Advisory Board:

Ahmad S.N. (FRCP); Ahmad S.Z. (FRCP); Allaqaband G.Q. (FRCP); Ashok Parihar (MD); A.Rauf (MD); A. Nafi (MD); A.R. Nasti (MS); Abdul Ahad (MD); Ahanger A.G. (Mch); Bhan B.M. (FRCS); Bharat Bushan (MD, DM); Banday Shafiq (FRCS); Biliquis S.J. (MS); Bashir Ahmed (MDS); B.A. Chappu (MD); Girja Dhar (FRCS); G.H. Hajini (MD); G.M. Shah (MD); Ghulam Hassan (MS); Gagan Singh MS; Mehmooda Khan (FRCS); M. Lajam (MRCP); M.Aslam (MS); Mohd. Al-Mofarah (FACHATZ); M. Syed (MD); M.A. Sofi (FRCP); M.S. Misger (MS); Mohd. Maqbool (MS); M.S. Shant (MS); M.A. Khan (MD); Mir G. A DMR; M. Lateef (MD); Mushtaq A. (MD); M. Ashraf (MD); M.Y. Kharadi (MD); Manzoor A Thakur (MD); Parveen Chesti (MD); Qazi Masood (MD); Rattan Parkash (MD); Rukhsana A (MD); S.N. Dhar (MD,FCCP); Suphia Snerbeeni (MRCP); Sanyal B.J. (MD); Sushil Razdan DM; Tara Singh (MS); T.S. Sethi (MS); Wazira Khanum (MS). Karamjit Dutta (MD) S.L. Verma (MRCP)

International Editorial Board:

Abdul Aziz Hagroo (KSA); Abdul Majid Hashia (JK); Azra Shah (UK); A.M. Rather (JK); A.A. Bhat (UK); Anil Bhan (Delhi); Anil Arora (Delhi); Ashaiq H.N.(JK); A.S.Sethi (JK); A.K.Jain (UP); A.A. Sheikh (JK); Altaf Hussain (JK); A.Wahid (JK); Bhat A.Salam (JK); Bhat Bashir A. (Aus.); Vijay Gupta (Jammu) M.R. Kotwal (Sikkim); Farida Shawl (JK); Ghulam Jeelani (JK); G.R. Nahimi (UK); G.R. Mir (JK); G.Q.Khan (JK); Gazanfar Ali (JK); Hamid Ali Durani (JK); H.S. Rissam (Delhi); Jallal S. (JK); Khurshid Iqbal (JK); K.L. Chowdary (JK); Kamal Ahmad (Aligarh); Mir Nazir (JK); Mohd. Megamzie (KSA); Manzoor Haroon (USA); M.Hussain (KSA); Mushtaq A. Margoob (JK); M.A. Akhtar (JK); M.A.Shah (USA); M. Salahuddin (JK); M.Yousuf (JK); M.A. Wani (JK); M.A. Lone (JK) Parveez A.Shah (JK); S.K.Gupta (Jammu) Shad Saleem (KSA); Shabir Qazi (KSA); S.Z. Mehdi (JK); Sheikh Ajaz (JK); Sheetal Singh (JK); Suhail R. (USA); Tajamul Hussain (JK); Tariq Nazki (UK); Tariq Azad (JK); Umar Javid (JK); Wani N.A. (JK). Malik G. Hassan (KSA); Sarfaraz Durrani (USA) Majid Aziz (USA), Suhail Allaqband (USA)Arshad Khalid Bhat (Dubai) M. Muzaffar Mir (JK) N.M Tiku Usha Koul (New Delhi), Imtiyaz Shah (JK) Yousuf Kanjwal (USA) Yaser Aslam (USA).

Editor-in-Chief

G.M. Malik, MD, FACG, Srinagar, Kashmir, India

P.O.Box 884, Pin Code 190 001 FAX 0091-0194-455592 Telephone No. (Resi) 0194-432060

E-Mail zakhatib@ nde.vsnl.net.in

Consultant Editors

USA: Farooque A.Khan, MB, MACP, FCCP, Arifa Khan ***M.D., New York***; Muzaffar Ahmad, MD, FCCP, ***Cleveland***; P.K. Shah, MD, FACS, ***Los Angles***; Fayaz A. Shawl, MD, FACC, ***Washington***; Farooq Peerzada MD, Ram Chutani, MD, FACS, ***Boston***; Ramesh Khardori, MD, MB, FACP, FACE, ***Illinois***, Khalid J. Qazi, MD, FACP, ***Buffalo NY***; Iftikhar A. Shah, MD, FACC, Peerzada Noor D.M., ***Ohio***. M.A. Shah MD, FACG ***Maryland***, G. Nabi Mir B. Sc; M. Pharm; PhD. ***Buckingham.Abdul Rauf Mir, Kansas***.

UK: Altaf Hussain, MS, FRCS; G.J. Mufti, DM, FRCP; G.R. Mufti, FRCS; M.A. Mir, FRCP; Nisar A.Mir, MRCP; Riyaz A. Banday, FRCS.

KSA: Mohammad Al Karawi, FA, ***Riyadh***; Ibrahim Al-Temimi, FA, ***Riyadh***; Abdul, Zakari Howsawi *Medina*, Aziz Al-Saigh, FRCS, FACS, ***Riyadh***; Abdul Majid, FRCS, ***Riyadh***. Fadel A. Razzak Khayat FRCS, ***Riyadh***.

New Zealand: Zahoor Ahmad MS.

Malaysia: Muhammad Yahya Alvi, MB, MRCP, FRCP.

India: ***New Delhi***: Rakesh Tandon, MD, Ph.D.; D.K. Bhargava, MD, DM; Upendra Koul, MD, DM, DNB; V.P. Venkatachalam, MS; ***Chandigarh:*** B.K. Sharma MD, DM; R.P.Sapru, MD, FICA; ***Aligarh:*** Arif Siddique, MRCP; ***Srinagar:*** M.S. Khuroo, MD, DM; Mehruj-ud-Din MD, FFARCS; Zubaida Jeelani, MD, DM. ***U.P*** S.R. Naik MD, DM , Ratni Gujral MD, FICR, H.L. Goswamy M.S., Phola Koul M.S., D.M.R.

Associate Editors (Hon.):

Mir Tanveer (USA); M.A. Jallu, MS, (UK); M.R. Teli (UK); R.K. Chrungoo, MS (Jammu); A.R. Khan, MD, (Kashmir); A.H. Zargar, MD, DM, (Kashmir); M.A. Kamili, MD, (Kashmir); M. Ahmad, MD, (Kashmir). Ghulam Nabi (KSA); Fayaz A. Fazili (KSA)

Executive Editor

Zaffar A. Khatib, MD, "Tabassum" Gogji Bagh, Srinagar, Kashmir Ph. (R) 430673. P.O. Box 1216 G.P.O. Srinagar 190 001 Kashmir E-mail zakhatib@vsnl.com

Deputy Editors (Hon.):

Riaz Bashir MD, Boston, (USA) Srinagar, Kashmir, India Fayaz A. Bhat, MD, Srinagar, Kashmir.

Assistant Editors: Gulzar A Hagroo UK, Showket Bashir, New York, Syed Amir (Kmr, Sgr.). Imtiyaz A. Shah M.S., Jammu. N.A. Bhat UK.

Advertising Executive:

M.L. Bhat, MD, Abi Guzar, Srinagar - 190 001, Kashmir (India) Ph.: 472672, 477077

Managing Editor:

Malik Suhail Post Box 884, Srinagar 190001, Kashmir India.

Computer Execution:

B.Q. Zaman & Mushtaq Ahmad at Gulmarg Computronics,

IInd Floor 92, Munir Manzil, Near Regal Cinema, Regal Chowk, Srinagar

Aims and Scope:- JK-Practitioner is a multidisciplinary Medical Journal published quarterly from Srinagar. Emphasis is placed on matters related to medicine in this country in particular, while articles from anywhere in the world are given due importance. Besides original articles and case reports the journal includes clinical reviews, guest articels and special articles on current aspects in medicine and therapeutics.

Copyright ©:- The publisher reserved throughout the world and in all languages. No part of this publication may be reproduced, transmitted or stored in any form or by any means either mechanical or electronic, including photocopying, recording or through an information storage and retrival system without the written permission of the copyright holder.

Although great care has been taken in compiling the contents of this publication, the publisher is not responsible or in any way liable for the currency of the information for any errors, omissions or inaccuracies or for any consequences arising therefrom. Opinions expressed do not necessarily reflect the views of the publisher, editor or editorial board. The publisher does not guarantee, warrant or endorese any product or service advertised in this publication nor do they guarantee any claim made by the manufacturer of such product or service.

JK-Practitioner: (ISSN 0971 - 8834) is ***Printed, Published and Owned by Dr. G.M. Malik and Printed at Afaq Printing Press Kashmir, and Published at Nowhatta Srinagar, Kashmir (INDIA). Editor-in-Chief Dr. G.M. Malik, MD, FACG,*** Tel. No. 0091-0194-432060 FAX 0091-0194-455592. Annual subscription price: Domestic Rs. 400 per year & rest of world equivalent to US $ 100 (Further details elsewhere in the journal).

INDEX VOLUME 6

JK Practitioner Vol 6 No. 1 January - March 1999

EDITORIALS

- Transanal Endoscopic Microsurgery 01 *O.J.Shah & Others*
- Coronary Heart Disease In Diabetes Mellitus - South Asian Scenario 02 *A.H.Zargar*
- Molecular Genetic Interventions 04 *Syed A.Tabish*

REVIEWS

- Tuberculous Meningitis 06 *SK Gupta & Others*
- Windows Of Blunt Trauma Abdomen - A Rational Approach 11 *F.M.Fazili*

MINI REVIEW

- Effects Of Exposure To Cold And Exercise On Bronchial Asthma 17 *PA Koul & Sunil Munshi*

GUEST ARTICLE

- Evidence - Based Medicine 24 *Tanveer Mir*

ORIGINAL ARTICLES

- Epidemic Dropsy In Jammu - Clinical Study and Review 28 *G.Ali & Others*
- Hydrocephalus In Children - Analysis of 50 Patients 32 *NC Digray & Others*
- Role Of Elective Irradiation To Drainage Sites In Squamous Cell Carcinoma Of The Skin Trunk And Extremities 35 *NA Khan & Others*
- Clinical Profile And Management Of Ectopic Pregnancy In Kashmir 39 *Bilquees & Others*
- Epidemiology Of Perinatal Mortality - A Hospital Based Study 41 *F. Fazili & GM Mattoo*
- Inguinal Hernia In Infants And Children In Kashmir India 46 *S.A.Malik & Others*
- Comparative Evaluation Of End Tidal Carbondioxide With Arterial Blood Gas Analysis 48 *Anjum Basu & Others*
- Haemodynamic, Biochemical And Haematological Profile During Transurethral Resection Of Prostrate. A Comparison Of The Effects Of Glyeine 1.5% And Distilled Water As Irrigating Fluid 51 *Rukhsana & Others*
- Double Blind Randomized Clinical Trial Of A Herbal Formulation "Optiliv" in Acute Viral Hepatitis 54 *NR Biswas & Others*

CASE REPORTS

- Testicular Pain In Acute Aortic Dissection 58 *S.Bashir & Others*
- Compensatory Hypoventilation With Hypercapnia In Metabolic Alkalosis In A Patient With Gastric Outlet Obstruction - A Unique Case Report 60 *M.Shareeff & Others*
- Patent Ductus Arteriosus In Sister And Brother With Congenital Hydrocele 62 *MA Kamili & Others*
- A Unusual Cause Of Dysphagia - A Large Cervical Osteophyte 64 *N.Bhardwaj & V.P.Venkatachalam*
- Chromosome Study In A Child With Ambiguous Genitalia 66 *S.Gupta & Others*
- Acrokeratoelastoidosis Of Costa - An Atypical Presentation 68 *Qazi M. & Others*
- Cleft Hand With Deafmutism 70 *Rauoof MA & Others*
- Chronic Traumatic Diaphragmatic Hernia In A Child - An Unusual Presentation 72 *G.N. Lone & Others*

EXPERIMENTAL MEDICINE

- Sweat Glands In Man And Horse 74 *A. Ahad & Others*

SHORT REPORT

- Prognostication Of Acute Renal Failure In Patients With Cholera 78 *PD Kiritchenko*

RESEARCH LETTERS

- Birth Weight In Relationship To Blood Groups 80 *A.Ahmad & I.Ali*
- Social Correlates Of Neonatal Septicaemia 81 *K.Hakeem & Others*
- A Study Of Nutritional Status Of Elderly Population In The Age Group (60-75 Years) In Srinagar City 82 *Yasmeen Khan*

CLINICAL GUIDELINES

- 1998 Management Recommendations For Sexually Transmitted DIsease 84 *BA Malik & Others*

CLINICAL IMAGE 92 *FA Khan*

STUDENT'S PAGE 93 *M.Yousuf*

JOURNAL SCAN 94

JK-Practitioner Vol.6 No.2 April - June 1999

EDITORIALS

◆ New Classification of Diabetes Mellitus 96 - *Romesh Khardori*

REVIEWS

◆ Irritable Bowel Syndrome 97 *GN Mir*
◆ Latest Radiomaging Techniques for Diagnosing Portal Hypertension: A Review Article with Special Emphasis on Sonographic Findings 101 *Basharat H. Shah & Tanveer Mir.*

MINI REVIEWS

◆ HIV-The Current and Future Epidemic. An Overview 104 *Gurpeet Singh & Others*
◆ Prevention of Sepsis in Neonatal Intensive Care Units (ICU) 108 *K. Sheikh & Others*

SPECIAL ARTICLE

◆ AFP Surveilance-A Strategy for Polio-Eradication 112 *Bashir Gaash & Others*

ORIGINAL ARTICLES

◆ Congenital Urethral Anamolies in Ano-Rectal Malformations 116 *NS Digray & Others*
◆ Hormonal and Surgical Management of Cryptorchidism 118 *M.Saleem & Others*
◆ Simple Ligation for Appendectomy. A better Choice than Stump Invagination 121 *M.S Misger & Others*
◆ Cancer and Pregnancy 125 *VP Gangadharan & Others*
◆ Histopathological Study of Chronic Calcifying Pancreatitis (CCP) from Kashmir Valley. 130 *Azra Shah.*
◆ Primary Paratesticular Malignancy. Histopathological Study. 132 *AR Khan & ND Chowdary*
◆ Some Epidemiological Features of Hypertension in Rural Kashmir 135 *Yasmeen Wani & Others*
◆ Incidence of Caesarean section-A Hospital Based Study 139 *M Farooq & K. Hakeem*

CASE REPORTS

◆ Holt-oram syndrome-Report of a family. 142 *AH Zargar & Others*
◆ Hydatid Cyst of the Brain-A Case Report and Review of Literature. 145 *MA Wani & Others*
◆ Sporadatic Occulopharyngeal Muscular Dystrophy with Optic Atrophy. 147 *SM Saleem & Others*
◆ Edward's Syndrome Baby with Porencephaly Born to a Toxoplasmosis Positive Mother. 149 *Mushtaq Ahmad & Others*
◆ Asymptomatic Long Standing Itrogenic Abdominal Foreign Body A Rarity. 150 *Parveen Malik & Others*

MORNING ROUND

◆ Patient with Cough Fever and Palpitation. 151 *R. Bashir & Tanveer Mir*

EXPERIMENTAL MEDICINE

◆ Pharmacokinetics of Diacetylmonoxime (DAM) After Intravenous Administration in Healthy and Dichlorovos Intoxicated Cow Calves. 153 *M. Sultana & AK. Srivastava*

SHORTS REPORTS

◆ Adrenal Insufficiency in Patients with Antiphospolipid Antibody Syndrome- A Review of Literature 155 *B.H Shah & Others*
◆ The Individual Volumanory and Structural Varations of the Stomach Due to the Homeostasis of the Organism. 157 VI Pivtorak

RESEARCH LETTER

◆ Hepato-Biliary and Pancreatic Ascariasis in Endemic areas 159 *MS Khuroo*

COMMENTARY

◆ Euthanasia - The Debate Goes On 160 *F A Bhat & Others*

PRACTITIONER'S COLUMN

◆ Anaesthesia at the Primary Health Centre 164 *A. Ahmad & J. Manzoor*
◆ Measles, Mumps, Rubella (MMR) Vaccine-New Strategies. 168 *M Farooq Mir & Others*

HISTORY

◆ History of Dialysis 170 *GR Nahami*
MEDICINE UPDATE 173 *F A Bhat*
PERSONALITY PROFILE *Muhammad Yahya Alvi* *175*
MEET THE PROFESSOR *Mahmooda Khan* *176*
CONFERENCE CALENDAR 178

JK-Practitioner Vol.6 No.3 July-September 1999

EDITORIALS

◆ Antibiotic Treatment of Acute Coronary Syndromes Fact or Fiction 179 *U Kaul & Others*

REVIEW

◆ Acute Liver Failure 182 *MS Khuroo*

MINI REVIEWS

◆ Current Status of Management of Coronary Disease 191 *HS Rissam & Others*

◆ Risk Factors and Prevention of Colorectal Carcinoma 194 *OJ Shah & Others*

ORIGINAL ARTICLES

◆ Sinus Histocytosis with Massive Lymphadenopathy 198 *VP Gangadharan & Others*

◆ Endopyelotomy verus Conventional Pyeloplasty in PUJ Obstruction 201 *HS Bhatyal & Others*

◆ Role of Radioimaging in Management of "Surgical Ascariasis" 204 IA Mir & Others

◆ Pulmonary Aspergilloma-Surgical Management 207 *AG Ahanger & Others*

◆ Electroencephlographic Changes in Migraine-A Study of 200 Cases 211 *SK Gupta & Others*

◆ Haemodynamic and Ventilatory changes during Laproscopic Cholecystectomy under General Anaesthesia 215 *A. Naqib & Others*

◆ Early Diagnosis of Neonatal Septicemia 218 *BA Charoo & Others*

◆ Testicular Lymphoma-A Histopathological Study of Twelve Cases 220 *AR Khan & ND Chowdhary*

◆ Medulloblastoma - A Pathological Study 223 *P Shah & A Shah*

◆ A Study of the Failure Cases of Sterilization in a Rural Area of Jammu 226 *C Vashnavi & Others*

CASE REPORTS

◆ Cranial Hyperostosis 229 *S Raffi* & T Mir

◆ Von Hippel Lindau Disease 232 *M Gupta & Others*

◆ Anaplastic Myeloma - A Report of Two Cases 234 *Gretha N. & Others*

◆ Omental Lipoblastoma 236 *NC Digray & Others*

◆ Angioma Serpiginosum 238 *Q. Masood & Others*

◆ Aorto Caval Fistula 239 *M Akbar & Others*

◆ Appendicitis Secondary to Foreign Body Impaction 241 *IS Mir & Others*

◆ A Case Report of Vesico Cutaneous Fistual 243 *Imtiyaz A. Shah & Others*

COMMENTARY

◆ Today the Sheep. Tomorrow the Shephard. Is the clock Tickling for a biological Hiroshima? 244 *MA Kamili & Others*

HOSPITALS TODAY

◆ Patient Satisfication Survey of Emergency Department At a large Teaching Hospital 247 *SA Tabish & Others*

STUDENT'S PAGE

◆ All Except 250 *Abdul Ahad*

JK-Practitioner Vol.6 No.4 October - December 1999

EDITORIAL

◆ The Electronic Highway in Medicine 251 *S.A.Tabish*

REVIEWS

◆ Advances in drug treatment of Non-variceal upper Gastrointestinal bleeding 253 *MS Khuroo & Naira K.*
◆ Flow Cytometry in Uro-Oncology 259 *K. Chithrathara & Others*
◆ Multiple Myeloma-Status of High Dose Stem Cell Transplantation 265 *V.P. Gangadharan*

MINI REVIEW

◆ Functional Constipation-Pharmacological and Naturopathic Perspectives 270 *G.N. Mir*

ORIGINAL ARTICLES

◆ Non-Psychiatrist Clinicians training in Psychiatry, its Perceived adequacy and modalities of treatment used 273 *M.Margoob & Others*
◆ Primary Lymphoma of Bone-Reivew of 56 cases 278 *A.Gupta & Others*
◆ Atlanto Axial Dislocation 282 M.A.Wani & Others
◆ Clinico-Radiological profile of spinal cord tumors 286 *Raja Zahid & Others*
◆ Abdominal Complictions of Ventriculo Peritoneal Shunts in children 289 *N.C. Digray & Others*
◆ Primary Duodenal Lymphoma. A Short Study of Six Cases. 292 *S.A. Aziz & Others*
◆ Sickle Cell Disease in Childhood 296 *G.Nabi*
◆ Polycythemia in Kashmiri New Born *299* *R. Hameed & Others*

CASE REPORTS

◆ HELLP Syndrome. A case study with review and recommendations 302 *A Bhat & KJ Qazi*
◆ Gaint recurrent Ventral hernia 305 *S. Iqbal & Others*
◆ Albendazole Therapy in Type III Hydatid Cyst Liver 308 *GN Yattoo & Others*
◆ Primary Adenocarcinoma fo the Small Bowel 310 *Anil K. Koul & Others*
◆ Bronchial Carcinoid-A Diagnosis on Fibreoptic Bronchoscopy 314 *GQ. Khan & Others*
◆ Pseudothalidomide Syndrome in Association with Intrauterine Infection 316 *GM Ladakhi & Others*
◆ Hereditory Multiple Exostosis 317 *Muzaffar Jan & Others*
◆ Dyschromatosis Universalis Hereditaria 318 *Qazi Masood & Others*

COMMENTARY

◆ Congenital Leukemia 319 M Hassan & M. Jan

CLINICAL IMAGE

◆ Spinal Arachnoid Cyst Presenting as Compression Paraparesis 321 SM Saleem & Others

HOSPITALS TODAY

◆ Radiation Safety Status in Nuclear Medicine Department of Sher-i-Kashmir Institute of Medical Sciences 322 *SK Koul & Others*

SPECIAL ARTICLE

◆ G.R. Memorial lecture - A Tribute to Our Teachers 326 *F.A. Khan & Others*

OVERSEAS DIARY

◆ Post Graduate training for Overseas doctors in the United Kingdom 330 *M.A. Mir*

JOURNAL SCAN

◆ Update in Allergy and Immunology 333 *Mark T. O' Hollaren*
Abstracts *337*

CONFERENCE REPORT

◆ International Conference on Recent Advances in Medicine - An Update 338 *G.M. Malik*

PERSONALITY PROFILE

◆ Ghulam Jeeiani Dhar 339

BOOK REVIEWS/CONFERENCE CLENDAR/OBITUARY

◆ 340

Transanal Endoscopic Microsurgery

Carcinoma of Rectum and some large villous adenomas are normally treated by Anterior resection of Abdominoperineal resection. Alternative methods have been sought which avoid major abdominal surgery. Palliation has been achieved with varying degrees of success by Interstital or external beam irradiation[1], electrocoagulation[2,3], chemotherapy[4], cryotherapy[5] and laser therapy[6]. Early cancers and benign rectal Polyps can also be completely removed by Transanal[7] or Transsphincteric excision[8].

Minimal access surgery has been thrust into prominence largely because of the success of laproscopic cholecystectomy and its many advantages. Transanal endoscopic microsurgery (TEM) is another outgrowth of minimal access surgery. The instrumentation and technique were developed by Buess etal[9] in Germany. it is a endoluminal, minimal invasive technique which allows the perianal excision of rectal lesions up to 20 cms above the anal verge, without major pelvic dissection or unnecessary resection of the rectum.

Flat villous tumours and very early cancers are candidates for peranal techniques. Traditional transanal procedures are mostly for technical reasons, limited to tumours in the distal 10cms of the rectum. Large tumours and those of upper rectum and distal sigmoid are virtually impossible to resect with the conventional transanal approach[10]. The Kraske and Mason techniques of transsphinteric surgery, while theoretical alternatives have been superseded by restorative anterior resection and are associated with a relatively high complication rate. Rectal excision while completely removing the lesion may have serious functional and physiological consequences.

The basic tool of TEM is a modified operating rectoscope optic and has four gas tight ports to allow simultaneous use of four instruments. The rectum is inflated with carbon dioxide which gives a good three dimensional view of the rectum and lower sigmoid. For posterior lesions the patients is placed in the conventional lithotomy position, but for anterior leasions the patients should be faced down with legs apart, held on support. Specially designed instruments, including curved scissors, curved tissue graspers, needle holders and a needle tip high frequency diathermy knife, cutting, haemostasis and suturing. Suturing is carried out with absorbable sutures using a silver clip on a special clip applicator as a substitute for surgical knots, and end to end anastomosis is possible.

The major advantages by this procedures are firstly it gives a clear three dimensional view secondly hand and eye coordination is easier, thirdly the dissection methods used are similar to those of conventional technique. Various excision methods are possible mucosectomy, partial thickness excision, or full thickness excision. The specific problems are first the limited space inside the human which makes suturing especially difficult. The second problem is that the equipment is expensive and cannot really be used for any other application and lastly staff needs proper training.

It is essential that the rectal cancer be examined by a endorectal Ultrasound to determine the depth of penetration into the rectal wall and the presence of lymph node matastasis. Endo rectal ultrasound is approximately 75 to 90% accurate in determining the depth of penetration, but is less effective in detecting lymph node matastasis[11]. If USG demonstrates deep penetration of the muscularis propia or extension to the prerectal fat, making local excision for cure unlikely then the radical recession may be preferable. It is stated that an indication of 1' TEM for cure in well or moderately well differentiated T1 carcinoma (Dukes A lesion infiltrating the submucosa only). Pt. with well or moderately well differentiated T2 carcinoma (Dukes A) infiltrating the muscularis propia) have a limited chance of cure with TEM resection alone, but the technique is ideal for the elderly who are reluctant to undergo a major resection[12]. This minimal invasive procedure may be used for palliative treatment at any tumour stage. Small low villous adenomas are easily excised Transanally, but extensive lesion are difficult to treat and in the past have required difficult Transanal excision[7], a parasacral approach[8], anterior resection or even abdominal perineal excision of the rectum. The high malignant potential of large villous adenomas and their potential to produce, profound electrolyte disturbance from mucous diarrhoea have justified this radical approach. These extensive adenomas are relatively simple to excise with the rectoscopy although several attempts are preferred. Many authorities have recommended TEM for patients with rectal villous adenomas[13,14]. The main operative problem is intrapertional perforation in up to 20% of patients, other problems are suture dehisecence and bleeding especially in very low and very high tumours. Late complications like stricture mostly after nonsegmental resection of semi-circumferential tumors and rectovaginal fistula in women after excision of anterior lesion.

We conclude that TEM is the method of choice for palliating patients with primary or recurrent rectal cancer and for treating patients with rectal villous adenomas. It is also an acceptable method for treating patients with small, early, protuberant, mobile rectal cancers with the expectation of cure and those with rectal cancers who are poor risks for major surgery.

Omer Javed Shah, MS. FAIS, FICS; *Smaeer Naqash*, MS.; *Manzoor Ahmad Dar*, MS, FRCS; *Prof. N.A. Wani*, MS, FRCS, FICS.

Department of General Surgery SKIMS, Soura, Srinagar.

JK-Practitioner 1999; 6(1) : 1-2

References:

1. Gunderson LL, Martin JK Beart RW. Intraoperative and external beam irradiation for locally advanced Colorectal Carcinoma. Ann Surg 1988; 207: 52-60.
2. Crile G, Turnbull RB. The role of electrocoagulation in the treatment of carcinoma of rectum. Surg. Gynecol Obstet 1972; 135: 391-6.
3. Eisenberg HW. Sequential electrocoagulation and resection for the carcinoma of the rectum. Surg. Gynecol Obstet 1984; 159: 471-4.
4. Yorkshire Gastrointestinal Tumour Group, Chemotherapy after palliative resection of Colorectal cancer Br. J.Surg 1984; 71: 283-6.
5. Osborne DR, Higgins AF, Hobbs KEF. Cryosurgery in the management of Rectal Tumour. Br. J. Surg. 1978;65: 859-61.
6. Bown SG Barr H, Matthewson K. Endoscopic treatment of inoperable Colorectal Cancers with Nd. YAG Laser. Br. J.Surg 1986; 73: 949-52.
7. Parks AG. Stuart AE. The management of villious tumours of the large Bowel. Br. J.Surg. 1973; 60:688-95.
8. Mason AY. Trans-Sphincteric exposure fo Rectum. Ann. R. Coll Surg. Engl. 1972; 51:330-31.
9. Buess G, Kipfmuller K, Ibald R. Clinical results of transanal endoscopic micro surgery. Surg. Endosc. 1988; 2:245-50.
10. Hermanck P, Gall FP. Early (microinvasive) Colorectal Carcinoma. Pathology, Diagnosis, Surgical treatment. Int. J. Colorectal Dis 1986;1: 79-84.
11. Waizer A, Zitron S, Ben-Baruch D, Bancel J, Wolloch Y, Dintsman M. Comparative study for preopertive staging of rectal cancer. Dys Colour Rectum 1989;32:53-6.
12. Buess G, Mentges B, Mannecke K, Starlinger M, Becker HD. Minimal invasive surgery in the local treatment of rectal cancer. Int. J. Colorectal Dis 1991;6:77-81.
13. Gaya J, Obrador A, Ozonas M, deSala E. Use of the urologic resectoscope in rectal pathology. Endoscopy 1983; 15: 260-2.
14. Irwin RJ. Resectoscopic Transanal resection of extensive Rectal Adenomas. Anst. NZJ Surg 1984;54: 375-7.

Coronary Heart Disease in Diabetes Mellitus - South Asian Scenario

Coronary heart disease (CHD) has emerged as the major cause of morbidity and mortality in most countries[1]. In India CHD accounts for 10-15% of all cardiovascular disease[2]. A number of risk factors which predispose a person to development of CHD have been identified. These include age, sex, hypertension, abnormal serum lipids, smoking, diabetes mellitus, impaired glucose tolerance and obesity. Obese type II diabetic patients invariably have associated lipid abnormalities which are not strictly normalized even by acceptable blood sugar control[3,4]. Uncontrolled diabetes mellitus is associated with increased platelet aggregation which plays an important role in the genesis of cardiovascular disease.[5].

Coronary events are more frequent in diabetic patients than in general population[6]. This is also true for unrecognized silent CHD in asymptomatic diabetic patients without a history of myocardial ischemia[7]. Insulin dependent diabetes mellitus (IDDM) patients with microalbuminuria have been reported to have an increased longterm risk of death from cardiovascular disease, which occurs as a concomitant feature with the development of clinical nephropathy[8]. People with non-insulin dependent diabetes mellitus (NIDDM) have age specific all-cause mortality rates approximately double than general population or nondiabetic controls.[9]

To determine the prevalence of CHD and asymptomatic electrocardiographic abnormalities (which is likely to be a consequence of silent myocardial ischemia in most cases) we analysed the case records of 2002 patients of diabetes mellitus admitted over a period of one decade to the endocrine services of a tertiary care centre. Among patients with NIDDM, 194 (11.61%) and 193(10.91%) had CHD and additional asymptomatic electrocardiographic changes respectively. IDDM was not associated with significant CHD and asymptomatic electrocardiographic changes (1 and 9 patients respectively). No patient with fibrocalculous pancreatic diabetes (FCPD) had clinical or electrocardiographic evidence of CHD. In an earlier study also we did not find any suggestion of CHD in subjects with FCPD[10]. There was a significant correlation between development of CHD and neuropathy ($p<0.01$), nephropathy ($p<0.01$), and retinopathy ($p<0.001$) in NIDDM patients. However, presence of hypertension in NIDDM patients steeply increased the risks of development of CHD (odds ratio 5.7). In an earlier sltudy we had found high incidence of CHD in diabetics with peripheral neuropathy[11].

Epidemiologic studies in migrant populations have clearly demonstrated that people of South-Asian origin have one of the highest incidence of CHD in the world[12,13]. Most of the studies performed in emigrant Indians have also documented that CHD frequently occurs at an early age and that it is diffuse and severe[13]. Established risk factors such as increased plasma cholesterol concentration, hypertension and, smoking do not explain the high mortality from CHD in these subjects[14]. Studies in Indian communities in the U.K have suggested that a higher prevelance of NIDDM, lower plasma HDL concentration and higher plasma triglyceride concentrations may be additional risk factors for CHD in this racial group[15,16]. The reported prevalence data of CHD in diabetic patients are quite varied. This variability could be due to different patient selection criteria and diagnostic approaches.

In Kashmir valley, 6.14% of people 40 years or above have diabetes mellitus and 8.09% have impaired glucose tolerance (unpublished personal data). Determining the mortality trends in diabetes mellitus, we found 16.6% patient have died of CHD in the last one decade at our centre[17]. With the better management of diabetes and possible decrease in infections and diabetes specific microvascular disease, we expect a high prevalence of CHD in our diabetics in decades to come. In view of the mammoth magnitude of diabetes mellitus, it becomes imperative to identify a high risk group who could be subjected to further invasive and non-invasive cardiac evaluation and management.

Professor Abdul Hamid Zargar, DM
Head, Department of Endocrinology,
Sher-i-Kashmir, Institute of Medical Sciences
Srinagar, Kashmir, India.
JK-Practitioner 1999; 6(1): 2-3

References:

1. Beaglehole R. International trends in coronary heart disease mortality, morbidity and risk factors. Epidemiol Rev 1990; 12:1.
2. Park JE, Park K. Cardiovascularr disease. In: Park's textbook of preventive and social medicine, 12th edn., Jabalpur, Banarasidas, 1983; 30.
3. Zargar AH, Majaaz BM, Masoodi SR, Laway BA, Dar FA. Serum cholesterol, triglycerides and total lipids in well controlled non-insulin dependent diabetes melitus. J Diab Assoc India 1991; 37: 37-40.
4. Zargar AH, Wandroo FA, Wadhwa MB, Laway BA, Masoodi SR, Shah NA. Serum lipid profile in non-insulin dependent diabetes mellitus associated with obesity. Int J Diab Dev Countries 1995; 15: 9-13.
5. Zargar AH, Koul S, Shah NA, Laway BA, Masoodi SR, Wandroo FA. Effect of glycemic control with insulin therapy on platelet aggregation in type 2 diabetes mellitus. Int J Diab Dev Countries 1996; 16: 84-86.
6. Pyorala K, Leasko M, Uusitupa M. Diabetes and atherosclerosis: an epidemiological view. Diabetes MEtab Rev 1987; 3: 463-524.
7. Cohn F. Silent myocardial ischyemia: classification, prevalance and prognosis. Am J Med 1985; 79: 2-6.
8. Borch-Johnsen K, Anderson PK, Deckert T. The effect of proteinuria on relative mortality in type 1 (insulin dependent) diabetes mellitus. Diabetologia 1985; 28: 590-596.
9. Tripathy BB, Keen H, Pickup JC, Talwalkar CV. Cardiovascular complications in Indian diabetics. Epidemiology of diabetes and its vascular complications, Ist edn, London: London IDF, 1978: 65.
10. Zargar AH, Laway BA, Masoodi SR, Shah NA, Shah JA. Fibrocalculous pancreatic diabetes from the Kashmir valley. Ann Saudi Med 1996; 16: 144-147.
11. Zargar AH, Sofi FA, Laway BA, Masoodi SR, Shah NA, Dar FA. Profile of neurological problems in diabetes mellitus: retrospective analysis of data from 1294 patients. Ann Saudi Med 1997; 17: 20-25.
12. McKeigne PM. Coronary heart disease in South Asians oversease. A review. J Clin Epidemiol 1989; 51: 597-609.
13. Enas EA, Mehta JL. alignant coronary artery disease in young Asian Indias. Thoughts on pathogenesis, prevention and therapy. Clin Cardiol 1995; 18: 131-135.
14. Gupta R, Prakash H, Majumdar S, Sharma S, Gupta VP. Prevalence of coronary heart disease and coronary risk factors in an urban population of Rajisthan. Indian Heart J 1995; 47: 331-338.
15. Hughes LD, Cruickshank J, Wright, Raftery EB. Disturbances of insulin in British Asian whitemen surviving myocardial infarction. Br Med J 1989; 299: 537-541.
16. Knight TM, Smith Z, Whittles A, et al. Insulin resistance, diabetes and risk markers for ischemic heart disease in Asian and non-Asians in Bradford. Br Heart J 1992; 67: 343-350.
17. Zargar AH, Wani AI, Masoodi SR, Laway BA, Bashir MI. Mortality in diabetes mellitus-data from a developing region of the world. Diab Research and Clinical Practice (in press).

Molecular Genetic Interventions

Gene therapy is a novel form of drug delivery that enlists the synthetic machinary of the patient's cells to produce a therapeutic agent. Using the body to treat its own disease overcomes the need to manufacture highly purified proteins. It also eliminates the need for repeated parenteral administration of proteins (as in hemophilia) or drugs (as in hereditary hypercholesterolemia) and reduces the difficulties of complying with exogenous-drug reigimens[1]. Applications of gene therapy are not limited to rare in-herited diseases but extend potentialy to common acquired disorders, including cancer, heart disease, and AIDS.

Now that it is becoming possible to map and establish the fine structure of human genes this knowledge has ushered in a new era in medicine. The applications of molecular biological techniques has enabled the dissection of many cellular control mechanisms, help in the investigation of both disease processes and the pursuit of prophylactic medicines and a variety of existing alternative therapies new halographgenetic engineering of human proteins has provided an important new approach to the treatment of, for example, many hemotological diseases and is proving useful in those instances where the disease results from the absence of a known protein. The isolation and cloning of many genes that code for these proteins are under way and the list of those that are already in clinical application is growing daily. Factor VIII, essential for normal blood clothing, was one of the first genes to be closed and is now joined by Interleukin 2 (IL-2), tumor necrosis factor (TNF) and the hemopoetic growth factors, such as erythropoetin and IL-3, to name but a few. The clinical application of Interferon A(IFN A) has proved valuable in the treatment of chronic myeloid leukemia and it is under trial in other myeloproliferative disorders as well as in myelomas[2]. Given that there are some 4000 different inherited gene defects known sofar, it is not perhaps surprising that many researchers feel that rather than replace a missing protein, the next logical step is to replace defective genes with normal ones.

The targets of gene therapy are either intracellular or extracellular. In the first example, the gene delivered to the cell affects the cell itself by replacing a defective or missing gene or by providing a product that kills or inhibits the growth of cells. In the second example, the cell releases the product of the new gene, which can act locally on neighbouring cells or enter the circulation for delivery to distant cells.

In theory, there are two routes by which genes may be introduced into a patient: by transfer, either into the germ cells, such as the sperm, eggs or early embryos, which can replicate; or into the normal somatic cells that cannot. Current ethics donot permit the former approach, but somatic cell therapy is well underway[2].

The best candidate for gene therapy are patients whose condition results from a defect in a single gene which resides in cellular material in a relatively accessible place. Defects in blood cells are therefore a promising possibility. The gene is delivered to its destination by viral infection. Because viruses must enter living cells to replicate, increasing attentioon has been paid to the use of genetically modified viruses-called vectors - as vehicles. The type of virus used is very much dependent upon the type of target tissue, the most commonly employed types being retroviruses and adenoviruses. The later vector is proving useful in transducing genes into cells of epithelial origin, such as those found in the bronchial airways of the lung and are employed precisely because the unmodified virus is a common cause of respiratory tract infections[2]. There are also nonviral methods of gene delivery. Liposomes, or lipid vehicles, which combine readily with cell membranes, are being used to deliver genes, some times as aerosols. Liposomes are also being tested in conjunction with viruses to enhance localised delivery of genes. Direct injection of naked DNA plasmids is possible, but for unknown reasons this method appears to function primarily in heart and skeletal muscle[1].

An important aspect of gene-delivery system is the ability to regulate the expression of the introduced gene, with the vectors that are now approved for gene therapy, cells express the gene continuously. As a result, the production of the therapeutic protein cannot be modulated. In diseases such as hemophilia regulation of the gene is not critical, but such diseases are the exception. In most other diseases, gene regulation is desirable: indeed constitutive expression of the introduced gene may be detrimental. To overcome this problem, yeast-gene or bacterial-gene regulatory systems have adapted for use in mammalian cells. The development of novel Vectors or vehicles for gene delivery warrants serious attention perhaps the ideal vector will be completely synthetic, a composits of DNA-Sequence Component derived from a number of existing Viral and plasmid vectors. Some desirable properties might include the ability to incorporate large genes, the absence of immunogenicity., the potential to direct, the vector to certain cell populations - possibly by incoorporating elements that recognise specific membrane components and enhance uptake- the ability to incorporate elements to limit the expression of the delivered genes to particular types of cells, and the ability to turn on or off and modulate the levels of gene expression in response to either non-mammalian exogenous regulators or endogenous signals such as hormones or glucose[1].

The triplex concept, is that single strands of DNA (oligonucleotides) will be introduced that should bind to selected segments of complementary DNA. The antisense approach employs oligonucleotides that bind to the messanger RNA. Both of these approaches should impede protein production[2]. One possible application that is currently being explored with antisease therapy is in the fight against the HIV. Antisense therapy is also under investigation as a treatment for hypertension.

Following on from the antisense approach is another similar method which employs the use of RNA enxymes called riboxymes. These can be synthesized to target specific genes involved in many disease processes and can be delivered to the site of action by the employing vectors. In addition to human cancer, the major clinical setting in which ribozymes have been investigated is in cobating AIDS.

Molecular tools have sparked a revolution in the diagnosis of genetic disorders. A molecular diagnosis can be made a well in advance of the appearance of clinical symptoms and can distinguish between disorders with similar phenotypes. Molecular diagnosis requires only a sample of DNA, which can be obtained from any source of nucleated cells, such as peripheral-blood lymphocytes or epithelial cells lining the buccal mucosa[3]. Molecular diagnosis testing will undoubtedly continue to grow in importance as more and more genes responsible for disease come to light. New forms of technology are being developed that will permit the simultaneous determination of a person's genotype at multiple loci. They will include not only loci responsible for rare genetic traits, but also those that contribute to subceptibility to more common disorders, including cancer, atherosclerosis, and hypertension. The landscape of preventive medicine will be changed dramatically, and the principles of genetics will become integral to day to day medical practice[4].

The potential for analysis of human disease is enormous and encompasses single gene disorders and multifactorial (Polygenic) diseases including cancer[5]. The human genome project is an attempt to systematise the research on mapping and isolating human genes that is already in progress in many countries, in order to create a single linear map of the human genome, with each coding gene defined and sequenced. The major objective of the Human Genome Diversity Project is aimed at increasing understanding of human evolution and to define the genetic relationships between human populations and interpret them in terms of natural selection, genetic drift, migration, etc[6].

Progress in gene therapy is being made and it looks likely to have an increasingly greater impact over the next decade in the fight against cancer and the correction of genetic abnormalities.

Dr. Syed Amin Tabish
MD. MAMS. FIMSA, FRIPH.
Fellow New Yoork Academy Sciences
Consultant & Medical Administrator
S.K. Institute of Medical Sciences
Srinagar (Kashmir).
JK-Practitioner 1999; 6(1): 4-5

References

1. Blau HM, Srinagar ML. Gene Therapy: A Novel Form of Drug Delivery. N Eng J Med. 1995: 333 (18): 1204-1207.
2. Will Court. Gene Therapy: Is There Hope After The Hype. New World Health. IHF, London 1997; 131-134.
3. Korf B. Molecular Diagnosis New England J Med. 1995; 332 (18): 1218-1220.
4. Korf B. Molecular Diagnosis (Part II). New England J Med. 1995; 332 (22): 1499-1502.
5. Yates JRW. Medical Genetics. BMJ. 1996; 312: 1021-1025.
6. World Health Organisation Technical Report Series No. 865: 1996.

Tuberculous Meningitis

S.K. Gupta MD;¯DM; Subash Gupta MD; Ashok Parinar MD. DM;

History

Robert Whytt initially described symptoms and signs of tuberculous meningitis (TBM) in 1768 and called this as "dropsy in the brain". He considered the collection of fluid in the ventricles as the disease itself, most likely because at the end of the eighteenth century the ventricles were regarded as the seat of the soul. Physicans at that time attributed somnolence and coma to a collection of fluid in the "seat of the soul" (i.e. acute hydrocephalus). By the end of the eighteenth century, investigators were beginning to shift their attention from the ventricles to the meninges.[1]

Tuberculous meningitis does not develop acutely from hematogenous spread of tubercle bacilli to the meninges. Rich and Mc Cordock[2] are credited with defining the aetiology of tuberculous meningitis after performing autopsy examinations of 82 cases of tubercular meningitis. Isolated miliary tubercles form in the parenchyma of the brain or the meninges during haematogenous dissemination of tubercle bacilli in the course of the primary infection or episodically during the course of chronic tuberculosis from endogenous reactivation of latent tuberculosis elsewhere in the body[3,4]. During the initial stage of infection, small numbers of millet-seed size tubercles are scattered throughout the substance of the brain and meninges. These tubercles tend to enlarge by confluence and growth and are usually caseating, that is, soft and exudative[5]. The propensity for a caseous lesion to produce meningitis will be determined by its proximity to the subarchanoid space (SAS) and the rate of which fibrous encapsulation develops due to acquired immune resistance[4]. Subependymal caseous foci may remain quiescent for months or years but then may cause meningitis via discharge of bacilli and tuberculous antigens into the subarachnoid space[3].

Clinical presentations of TBM:

The clinical manifestations of TBM is either that of an acute meningitis syndrome characterized by coma, raised intracranial pressure, seizures and focal neurological deficits or that of a slowly progressive dementing illness. When the infection presents as an acute meningitis syndrome, characteristic signs and symptoms are headache, malaise meningismus, papilloedema, vomiting, confusion, seizures and cranial nerve deficits. Patients admitted with lethargy or stupor may become comatose in a matter of days. Fever may or may not be present.

Tuberculous meningitis may also present as a slowly progressive dementing illness with memory deficits and personality changes typical of frontal lobelike disease i.e. abulia, urinary and faecal incontinence. This is more common presentation of TBM. Cranial nerve deficits and convulsions also occur in the subacute form of TBM[4]. There is often a history of anorexia, cough, night sweats and weight loss days to months prior to the development of symptoms of central nervous system infection[6].

Table 1" Showing signs and symptoms of tuberculous meningitis

Symptoms	Signs
Prodromal	
Anorexia	Adenopathy-most commonly cervical
Weight loss	Adventitious sounds on auscultation of lungs (apices)
Cough	Choroidal tubercles
Night sweats	Fever (highest in the late afternoon)
Headache (worse in recumbency)	Nuchal rigidity
Meningismus	Papilloedema
Altered level of consciousness	Focal neurological signs
	Positive tuberculin skin test.

A tuberculous encephalopathy is also described. This is a syndrome of convulsions, stupor or coma, involuntary movements, paralysis and decerebrate spasms or rigidity with or without clinical signs of meningitis or C.S.F. abnormalities or tuberculous meningitis. Pathologically there is either diffuse oedema of cerebral white matter with loss of neurons in gray matter, a haemorrhagic lukoencephalopathy, or a post infectious demyelinating encephalomyelitis. The syndrome has been observed primarily in children with miliary or disseminated tuberculosis[3,7].

Risk factors for tuberculous meningitis include age,

JK-Practitioner 1999; 6(1): 6-10

From the Department of Medicine (Gupta, Subash, Prof. Parihar) **Govt. Medical College, Jammu (India)**
Received August 1998 Accepted January 1999
Correspondence to : Dr. S.K.Gupta, 718-A, Gandhinagar, Jammu (Tawi)-180 004

alcoholism, infection with human immuno-deficiency virus, malnutrition, state of immunodepression, drug abuse and homelessness.

Table, 1 gives signs and symptoms of TBM.

Complications of Tuberculous meningitis

The neurologic complications of tuberculous meningitis are initiated by a hypersensitivity reaction to the discharge of tubercle bacilli and tuberculous antigens into the subarachnoid space. This leads to the production of a thick exudate that fills the basilar cisterns and surrounds the cranial nerves and major blood vessels at the base of brain, constricting the vessels that comprise the circle of Willis. With in a matter of days, a proliferative arachnoiditis develops. The presence of an inflammatory exudate in the basilar cistern obstruct the flow of C.S.F., with resultant obstructive hydrocephalus and blocks resorption of CSF by the arachnoid granulations as fibrous adhesions develop. Communicating hydrocephalus develops as the resorption of CSF is blocked. Cerebral ischaemia and infarction develops as result of vasculitis due to a direct invasion of arterial walls by mycobacteria or compression of the blood vessels at the base of the brain from the adjacent arachnoiditis. Regardless of the aetiology, intracranial vasculitis is a major factor contributing to morbidity and mortality from tuberculous meningitis[4].

Table II Showing the complications of TBM.

- Convulsions
- Cranial nerve deficitis (Oculomotor, optic, vestibulocochlear, abdusence, trochlear, facial).
- Strokes- Hemiplegia, monoplegia
- Mental defects
- Growth retardation
- Hydrocephalus
- Hypothalamic disturbances, obesity, hypogonadism, frolich's syndrome, sexual precocity, diabetes inspidus.
- Spinal arachnoiditis leading to myeloradiculopathy.

Diagnosis of T.B.M.

The diagnosis of TBM is based on a strong clinical suspicion and laboratory data that suggest the diagnosis. The initiation of therapy should not await bacteriologic proof of tubercle bacilli by smear or culture.

Radiologic evidence of pulmonary tuberculosis specifically hilar adenopathy, is found in 50 to 90% of tuberculous meningitis in children[8,9]. Zarabi et al[10] evaluated the chest roentgenogram abnormalities in 180 children with TBM, ranging from one month to 15 years. Forty six children (26%) had changes consistent with primary intrathoracic-hilar and/or mediastinal adenopathy, cavities, pneumatoceles and calcification in the hilar area. Twenty three children (13%) had x-ray findings of disseminated miliary pattern with a primary complex and 15 (8%) had areas of intrathoracic calcification. In adults, however, the association of pulmonary lesions and meningitis is not as high, and the absence of pulmonary disease should not rule out tuberculous aetiology for the aseptic meningitis[9,10].

The intradermal tuberculin skin test is helpful when positive. The test may, however, be falsely negative even in the absence of immunosuppression and in association with a positive reaction to the common antigens used to determine anergy, i.e., candida and mumps. The tuberculin skin test has been reported to be negative in 50-70% of cases and often becomes positive during the course of therapy[3,11].

Communicating or obstructive hydrocephalus, basilar meningeal enhancement following contrast administration and cerebral infarction are the most frequently reported computed tomography and magnetic resonance imaging abnormalities in TBM. In large series, hydrocephalus is present in 59-76% of cases, meningeal enhancement in 64% of cases and cerebral infarction in 17-53% of cases. Tuberculoma is less common finding and is present in 10-28% of cases[12,13,14]. Hydrocephalus is so frequently a complication of tuberculous meningitis in children that, prior to the identification of the tubercle bacillus by Robert Koch in 1882, the diagnostic term most often used for tuberculous meningitis in children was acute hydrocephalus.[15]

The various diagnostic tests under taken for diagnosis of TBM are listed in table III.

Table III: Showing diagnostic studies in TBM.

1. Tuberculin Skin test
2. Chest X-ray
    - Hilar adenopathy
    - Upper lobe nodular infiltrate
    - Miliary pattern
3. Computed tomography or magnetic resonance imaging.
    - Hydrocephalus
    - Basilar meningeal enhancement post-contrast
    - Cerebral infarction
4. Eye examination for choroidal tubercles
5. Sputum and urine smear and culture for acid fast bacilli.
6. C.S.F. examination.
    - Elevated opening pressure
    - Elevated protein concentration in the range of 100-500 mgm/dl.
    - Decreased glucose concentration
    - Increased white blood cell count between 10-500 cells/cubic mm with a predominance of lymphocytes.
    - Decreased chloride concentration
    - Low serum/C.S.F. bromide ratio
    - Positive tuberculostearic acid assay

- ★ Culture positive in 75% of cases requiring 3-6 weeks for growth.
- ★ Postive polymerase chain reaction (PCR)

CSF abnormalities in TBM

At an early stage in the clinical illness there may be very few WBCs in the C.S.F. or polymorphonuclear leukocytes may predominate initially with lymphocytes becoming the predominent cell type within 48 hours. A mild elevation in the protein concentration in the C.S.F. with only a few cells present is compatable with TBM.

Repeat examination of C.S.F. will most likely demonstrate a progressive increase in the protein concentration, a progressive decrease in the glucose concentration and shift to a mononuclear pleocytosis. In addition, there may be a shift in the cell type in the C.S.F. following the initiation of antituberculous therapy from an initial lymphocytic pleocytosis to a predominance of polymorphonuclear leukocytes[4,6].

The acid fast bacilli can be demonstrated in c.s.f. if examined carefully and repeatedly. They are best demonstrated in smear of the clot or sediment. If no clot forms, the addition of 2ml of 95% alcohol results in a heavy protein precipitate which on centrifuging draws bacilli to the bottom of the tube. The centrifuged deposit of c.s.f. can then be examined on a glass slide for the bacilli. Positive smears are typically reported in only 10-40% of cases[16,17].

The most successful technique for identifying the organism requires centrifuging 10-20 ml of c.s.f. at 2500 RPM for 30 minutes and then preparing a thick smear from the pellicle for examination. The smear is then examined for 30-90 minutes. Using this technique, organisms have been identified in 91% of TBM in one series and 35%, in the another. This emphasizes the importance of examining the smear for at least 30 minutes[3,18,19].

Cultures of c.s.f. requires 3-6 weeks for growth to be detectable and are positive in approximately 75% of cases of TBM[4].

The c.s.f. chloride concentration and the bromide partition test have been disappointing in differentiating tuberculous meningitis. The c.s.f. chloride concentration may be decreased in TBM to less than 110 meg/L, however, this is a nonspecific abnormality.

The bromide partition test measures the ratio of serum/C.S.F. bromide 24 hours after the oral administratioin of sodium bromide or the intravenous infection of radio active bromide[20]. In patients with TBM, the ratio of serum/C.S.F. bromide will be low. A low bromide partition ratio is, however, not specific for TBM and simply represents an increase in the permeability of the blood-C.S.F. barrier.[3]

The determination of C.S.F. adenosine deaminase may be helpful in distinguishing CNS tuberculosis from bacterial meningitis but again is not specific for TBM. The concentration of tuberculostearic acid in spinal fluid has been reported to be a sensitive marker for CNS tuberculosis, but this analysis must be obtained through the Centres for Disease Control as it is not available in most commercial laboratories.

The enzyme linked immunosorbent assay (ELISA) has been used in the laboratory to detect mycobacterium tuberculosis antigen and anti-mycobacterial antibodies in spinal fluid. The sensitivety of detection of mycobacterial antigen in C.S.F. by ELISA in different studies ranges from 60-100% and specificity of the test is from 80-100%.

Radio immunoassay (RIA) is a highly sensitive method and has been employed to detect mycobacterial antigen and antibody in C.S.F. as well as circulating immune complex (CIC). It is reliable and reproducible but the reagents are costly, have short half life and their handling and disposal pose special problem due o radiation hazards. The equipment required for reading is expensive and high level of technical skill is mandatory for obtaining reliable results. Therefore the use of RIA is restricted to the most advanced laboratories.

The polymerase chain reaction (PCR) technique for detection of tubercle bacilli DNA in C.S.F. is another method of diagnosis of TBM. In the laboratory this technique amplifies the mycobacterial DNA allowing for identification of the M. tuberculosis genome within 24-72 hours[21,22]. The rates of false positive and false negative results and the predictive value of the test are not yet known and therefore, the PCR assay for the rapid detection of M. tuberculosis is not yet recommended for routine clinical use[23].

Treatment of tuberculous meningitis

A combination of three antituberculous drugs is recommended for the treatment of TBM in adults. It is initiated as following:-

1. Isoniazid 5mg/kg/day, maximum upto 300 mg/day.
2. Rifampin 10mg/kg/day, maximum upto 600 mg/day and
3. Pyrazinamide 15-30 mg/kg/day, maximum dose 2gm/day.

Pyridoxine 50mg/day is given with INH to prevent the development of peripheral neuropathy.

In cases where antimicrobial resistance is suspected, ethambutol 15-20 mg/kg/day can be used in the inital regimen. If the clinical response is fairly good, pyrazinamide and ethambutol can be discontinued after 8 weeks and isoniazid and rifampin continued alone for the remaining 9-12 months[24,25].

Individuals infected with HIV, the recommended regimen is:-

1. INH 10-15mg/kg/day
2. Rifampin 10-15m/kg/day
3. Ethambutol 25mg/kg/day or
   Pyrazinamide 20-30mg/kg/day
4. Streptomycin 20-40mg/kg/day or
   Rifabutin or clofazimine.

Treatment in HIV infected patient is continued for atleast 6-9 months and at least 6 months beyond the demonstration of negative cultures.[25]

For TBM in children, the American Academy of Paediatrics recommends a 12 months regimen using the following antituberculous drugs.

1. INH 10-15mg/kg/day
2. Rifampin 10-20 mg/kg/day
3. Pyrazinamide 20-40mg/kg/day
4. Streptomycin 20-40mg/kg/day

The combination of INH, rifampin, pyrazinamide and streptomycin is continued for 2 months, followed by INH and rifampin administred daily or twice weekly under medical supervision for 10 months. When INH is administred twice weekly the dose is 20-40 mg/kg/dose and when rifampin is used twice weekly the dose is 10-20 mg/kg/dose. The American Academy of Paedietrics recommends that liver function be monitored during first few months of treatment. They also suggested administration of corticosteroids in cases of TBM.[26] Dexamethasone may be administred in a dose of 0.3-0.5 mg/kg/day in the first week of treatment followed by prednisolone 2mg/kg/day, tapered gradually over 3-4 weeks.[27].

Table IV: Shows antituberculous chemotherapy[26]

Drug	Dosage	
	Children	Adults
Isoniazid	10mg/kg/day once daily	300 mg/day
Rifampin	10mg/kg/day	10mg/kg/day
Ethambutol	15-25mg/kg/day in divided doses	15-20mg/kg/day in divided doses
Pyrazinamide	30mg/kg/day in divided doses	30mg/kg/day in divided doses
Streptomycin	20-40mg/kg/day once daily	1gm once daily

Indications of steroids in TBM

Steroids reduce meningeal inflammation and ocular complications. The following are the indications of using steroids in TBM[3]:

1. Altered consciousness
2. Papilloedema
3. Focal neurologic deficitis
4. C.S.F. opening pressure greater than 300 mm of water.

It has been seen that use of steroids reduces significantly mortality, neurologic complications and a significantly more rapid normalization of the C.S.F. white blood cell count, protein and glucose concentration. They also reduce ocular complications in patients with tuberculous meningitis[28].

Prognostic factors in TBM

The most important prognostic factor that is reported repeatedly in cases of TBM is the level of consciousness at the initiation of therapy. the greater the alteration in mental status, the worse the outcome. The mortality rate of patients who are comatose prior to the initiation of therapy is 50-70%[3].

Other factors that may adversely affect outcome include:-

1. Age (the mortality rate is highest in the very young and the very old)
2. Malnutrition.
3. The presence of miliary disease
4. The presence of an underlying debilitating disease such as alcoholism
5. Hydrocephalus
6. Cerebrovascular complications
7. Low C.S.F. glucose concentration
8. Elevated C.S.F. protein concentration

In patients with HIV infection, the duration of illness prior to the institution of therapy and a low total CD 4+ cell count are the most significant prognostic indicators.

To conclude TBM is a treatable disease and institution of early therapy helps the outcome of disease. The level of consciousness at the initiation of therapy is the most important prognostic factor in TBM.

References:

1. Mullener ER. Six Geneva Physician on Meningitis J. Hist. Med. 1965. 2: 1-3.
2. Rich, AR, McCordock. HA. The pathogenesis of tuberculous meningitis Bull Johns Hopkins Hosp. 1933; 52: 5-37.
3. Molavi A, Lefrock, JL. Tuberculous meningitis Med Clin. North Amer 1985; 69: 315-331.
4. Lenoard, J.M. Des Prez, P.M. Tuberculous meningitis Infect Dis. Clin. North Amer 1990; 4: 769-797.
5. Slavin, ER, Walsh J.J., Pollack, A.D. Late generalized tuberculosis A clinical and pathological analysis and comparison of 100 cases in the preantibiotic and antibiotic eras. Medicine 1980; 59: 352-366.
6. Newton, R.W. Tuberculous meningitis Arch. Dis. Child 1994; 74: 364-366.
7. Udani. P.M. Dastur, D.K. Tuberculous encephalopathy with and without meningitis clinical features and pathologic correlation, J. Neurol Sci 1970; 10: 541-561.

8. Lee, T.Y., Brown, H.W. Tuberculous meningitis patients as index cases in the epidemiology of tuberculosis. Am. J. Public Health 1968; 58: 1901-1909.
9. Lincoln, E.M., Sordillio, V.R., Davies, P.A. Tuberculous meningitis in children, a review of 167 untreated and 74 treated patients with special reference to early diagnosis. J. Paediatr. 1960; 57: 803-823.
10. Zarabi, M., Sane, S., Girdany, B.R. The chest roentgenogram in the early diagnosis of tuberculous meningitis in children. Am. J. Dis. Child. 1971; 121: 389-392.
11. Berenguer, J., Morene, S., Laguna, F., Vicente, T. Tuberculous meningitis in patients infected with the human immunodeficiency virus N. Engl. J. Med. 1992; 326: 668-672.
12. Teoh, R. Humphries, M.J., Hoare, R.D., mahony, G. Clinical correlation of CT changes in 64 chinese patients with tuberculous meningitis. J. Neurol, 1989; 236: 48-51.
13. Kingsley, D.P., Hendrickse, W.A., Kendall, B.E. Swash, M. Singh, V. Tuberculous meningitis: role of CT in management and prognosis. J. Neurol-neurosurg. Psychiatr 1987; 50: 30-36.
14. Price H.Z., Danziger A computed Tomography in cranial tuberculosis. Am. J. Roentgenol 1978; 130: 769-771.
15. Meindl, J.L. Menidl Co.l Tuberculous meningitis in 1830s. Lance (8271): 1982; 554-555.
16. Hass, F.J., Madhavan, T., Quinn, E.L. Tuberculous meningitis in an urban general hospital Arch. Inter Med. 1977; 137: 1518-1521.
17. Hinman, A.R. Tuberculous meningitis at cleveland Metropolitan General Hospital. 1959-1963 Am. Rev. Respir Dis. 1967; 95: 670-673.
18. Stewart, S.M. The bacteriological diagnosis of TBM. J. Clin Pathol. 1953; 6: 24-242.
19. Illingworth R.S., Miliary and Meningeal tuberculosis: Difficulties in diagnosis Lancet 1956; 2: 646-649.
20. Wiggelinkhuizenn J. and Manh, M. The radioactive bromide partition test in the diagnosis of TBM in children J. Paediatr. 1980; 97: 843-847.
21. Yuk-Fong Liu P. Shi ZY., Lau, YJ., Hu, BS, Rapid diagnosis of tuberculous meningitis by a simplified test Amplification protocol. Neurology 1994; 44: 1161-1164.
22. Folgnerir, L.Delgado, R., Palenque, E., Nuriega, A. Polymerase, Chain reaction for rapid diagnosis of TBM in AIDS patients. Neurology 1994; 44: 1336-1338.
23. Macher, A., Gssby, E. PCR & the misdiagnosis of active Tuberculosis. N. Engl. J. Med. 1995; 332: 128-129.
24. Snider D.E., Rieder, H.L., Combs, D., Bloch, A.B., Hayden, C.H. Tuberculosis in Children, Paediatr, Infect, Dis. J. 1988; 7: 271-278.
25. Holdiness, M.R. Managementof TBM. Drugs 1990; 39(2): 224-233.
26. Committee on Infectious Diseases Chemotherapy for tuberculosis in infants and children Pediatrics. 1992; 89: 161-164.
27. Jacobs, R.F., Sunakorn, P. Chotpitayasunonah, T. Pope S. Kelleer K. Intensive short course chemotherapy for tuberculous meningitis. Pediatr. Infect. Dis. J. 1992; 11: 194-198.
28. Girgis N.I. farid, Z. Kilpatrick, M.E. Sultan; Y. Mikhail, I.A. Dexamethasone adjunctive treatment for TBM. Pediatr, Infect. Dis J. 1991; 10: 179-183.

Windows of Blunt Trauma Abdomen

Fiaz Maqbool Fazili, MBBS, MS, MAMS, FICA; FICS (USA)

Trauma remains the leading cause of death and disability in first four decades of life around the world. Majority of victims is due to road traffic accidents, blunt injuries are the commonest and often involve multiple serious injuries. Deficiencies in the services for managing the severely injured patients have been frequently reported[1,2] leaving a scope of improvement from time to time. The purpose of this article is to outline a comprehensive approach to trauma care, to provide a framework for therapy, to highlight critical decision points, and to focus on selected key diagnosis and interventions on the basis of four trauma care themes. First, effective trauma care begins in the field and ends with discharge from rehabilitation .The final outcome reflects the aggregate care provided, and it is the surgeons responsibilty to be familaiar with all phases of trauma care . Second ,effective trauma care involves the dedication of a multi disciplinary team. The final outcome reflects the ability of the surgeon to coordinate the activities of many health professionals. Third, effective trauma care requires both speed and accuracy in the identification of all injuries and co- morbid factors that may be deranged. All members of the trauma team should be familiar with one systematic approach to evaluation of the patient, lest errors of omission in diagnosis and therapy lead to excess morbidity and mortality. Fourth effective trauma care hinges on speed, accuracy and appropriate prioritization of interventions. In contrast to elective surgical care identification of life threats and emergency intervention must be performed within the first few minutes of a patient encounter. These four themes suggest that most successful outcomes are obtained when acknowledgeable and skilled surgeon leads a cohesive team each member of which has a specific responsibility and whose collective team effort results in timely identification and address of life threats a complete injury inventory, and an appropriately prioritized plan of care.[3]

The abdomen extends from the diaphragm down to the pelvic cavity. The diagnosis of significant intraabdominal injury is one of the most difficult problem in the management of trauma. In some patients who are stable there may be classical signs of peritonitis on physical examination, celiotomy is warranted without further confirmatory diagnostic study. Failure to recognize and treat occult hemorrhage is not an uncommon mistake, injury may not be evident on initial examination or only an area of localized tenderness is found. With repeat examination, increasing abdominal tenderness, decrease in bowel sounds or involuntary muscle rigidity may become apparent. Haemorrhage may be suggested by haemodynamic instabilty or a slowly falling haemtocrit level. Gastrointestinal perforations usually manifest late with signs of peritonitis. Peritonitis from a bowel injury may lead to "third spaceing" (Plasma sequestration) and a rise in haematocrit level. The magnitude of progression may indicate the need for exploration. If that need is obvious, further diagnostic studies are indicated.[4] To rely on clinical history and physical examination alone in trauma setting is dangerous as nearly 50% cases may have no complaints or any external signs of abdominal trauma on arrival to the hospital[5].Thus necessitating rapid assessment and appropriate treatment of potentially life threatening conditions. The perplexing question in a truma set up is to answer the question whether an intraabdominal injury has occurred rather than what the abdominal injury is. The problem is detecting those with significant but occult injuries among the vastly greater number of patients who will not benefit from exploration. More problematic is the patient who has sustained a blunt injury, and if the patient is awake, alert and not toxicated, has no abdominal complaints, and is not scheduled to undergo an anesthetic that would interfere with abdominal examination. Serial abdominal examination, serial haematocrit determinations is a cost effective strategy to exclude serious abdominal injury. Such patients are rare . All others require objective evaluation, according to three scenarios.

1 The first scenario is the unstable patient whose injuries are confined to the abdomen ; such patients require immediate celiotomy.

JK-Practitioner 1999; 6(1): 11-16

From the Department of Surgery, King Fahad Hospital, Medina Munawarah, Saudi Arabia (Fazili)
Received August 1998 Accepted December 1998

Correspondence to : Dr. Fiaz Maqbool Fazili, P.O.Box 5147, Medina Munawarah, Kingdom of Saudi Arabia

2 Second scenario is that of a critically and unstable patient with multiple injuries, having haemodynamic instability, and uncertainty as whether abdomen is the site of the most severe (i.e. shock causing) injury. In this case, the preferred diagnostic technique is diagnostic peritoneal lavage.

3 Third scenario is that of a multiple injured but relatively stable patient in whom an abdominal injury, even if it exists does not constitute an immediate life threat. In this scenario CT scan provides useful information regarding not only the existence of an injury but also the probability that celiotomy will be therapeutic in these patients. Rapid assessment and appropriate treatment of potentially life threatening conditions is therefore mandatory.

The last decade has witnessed several major advances in the management of solid organ injuries. Among these has been the non operative management of selected adult or pediatric patients who has sustained blunt abdominal trauma. Initially this approach was viewed with skepticism and at best a modicum of enthusiasm has been over the past few years, been accepted as the current preferred method of treatment in those patients meeting inclusion criteria with the use of available diagnostic modalities. The present article reviews the role and rational use of paracentesis, DPL (diagnostic peritoneal lavage), US (ultrasound), CT (computed tomography) and Laparoscope in the management of blunt abdominal trauma. Diagnostic paracentesis and four quadrant tap were considered to be effective in the diagnosis of intraperitoneal bleeding due to injury apart from acute abdominal conditions such as primary peritonitis, acute pancreatitis. When correctly applied in cases of blunt abdominal trauma, it was predictive of significant injury when positive ,with an accuracy rate of 80 percent with minimal complications[6]. Unacceptable rate of false negative results as reported in various studies pushed it to disrepute[7]. The strong arguments against this time old bed side procedure was its serious limitations that a needle tip cannot reach the fluid collections giving rise to false negativity. The fact that localized collections of blood can occur in upper abdomen without reaching the pelvis and to obtain a small amount as a representative sample large volumes of blood must be present[8].

DPL: In an attempt to improve the diagnostic validity of abdominal paracentesis, Root et al in 1965[9] reported the use of DPL in patients who sustained blunt trauma abdomen. DPL is considered by many as the most important investigation for the early detection of intraperitoneal injury. The indications for DPL have been somewhat liberal in many studies and more selective in others. Depressed sensorium and altered pain response leading to false negative physical examination. Unexplained signs of shock (hypovolaemic), equivocal abdominal findings, impractical abdominal examination, major thoracic injuries especially lower rib fractures, major orthopedic injuries, fracture pelvis or spine, impractical abdominal examinations when patient is going for general anesthesia for nonabdominal emergency conditions are widely accepted indications[10]. An existing indication for laparotomy is the only absolute contraindication for DPL. While previous abdominal operations and advanced pregnancy are no longer considered absolute contraindications, although adhesions due to previous operations increases the risk of iatrogenic injury to the bowel and may also prevent free passage of catheter or mixing of the irrigating fluid with the intraperitoneal collection. The choice of lavage technique open or closed depends on body habitus, clinical situation, familiarity with the technique and expertise of the performer. Abdominal distention, previous abdominal operations, established pregnancy, evident portal hypertension, and established coagulopathy should be considered indications for the open technique, as direct visualization is essential to avoid serious complications and false positive results. Gross obesity should be an indication for a percutaneous technique as large amount of anesthetic and extensive incision and dissection are associated with considerable morbidity[11]. Patients with pelvic fractures are associated with huge retroperitoneal hemorrhage because the haematoma spreads up behind the alba causing the false positive results[12]. Open and percutaneous techniques have been used in pediatric injuries with accuracy rates similar to those adults, using a 14—gauge plastic sheathed needle with side holes cut by a scalpel as a catheter[13] if pediatric peritoneal lavage catheters of different sizes are not available. The presence of any amount of blood has been considered positive by many whereas others accepted 5 to 10 ml as an indication for laparotomy[14,15]. Haematocrits greater than 1 percent[12] and the inability to read newsprint through the tubing[16] has also been considered as grossly positive finding besides RBC count>100,000/cumm,WBC>500/cumm, faecal contamination,amylase>20IU/l, alkaline phosphatase (ALP>3U/L.). The combination of amylase (AM) >20IU/L and ALP>3Iu/L has been found to have positive predictive value of 88% for significant abdominal injury[17].If the effluent is faintly coloured quantification of RBC is done ,as change of colour can be seen as little as 0.25 ml of blood in 1000ml of solution . 1ml of blood yields a rise of 5000-10000 RBC /cumm in the lavage return and 20ml give a clearly positive results qualitatively and quantitatively. If the effluent is clear, WBC count is necessary. Elevation of WBC count alone as a positive finding occurs in 1-6% of all DPL, count of >500 cells/cumm is associated with injury to peritoneum caused by mechanical or chemical injury and bacterial infections. Using WCC (white cell count) as a sole positive lavage criteria was challenged by Jacobs[18] as only four out of 29 blunt injury victims in his study underwent laparotomy on admission. The WCC has been utilized in the early detection of small bowel perforation with an accuracy rate of at least 85 percent. As significant elevations of WCC occur only three hours from injury, WCC in DPL fluid is of no diagnostic value in victims of blunt abdominal injuries who are lavaged within 4 hours of injury[19]. The isolated intestinal injury is one of the common causes of false negative lavage. ALP (alkaline phosphatase) quantification ranging between 3-10 in lavage fluid was recommended to be of help[17] however false positive results have occurred in patients with pelvic fractures without bowel perforation. Lavage counts of 5000 to 100,000 RBC /cumm and WCC of 100 to 500/cumm are considered indeterminate and are found in2-6% of DPL .The fallacies in RBC count in a range of 20,000 to 100,000/cumm as a determinant of intraabdominal catastrophe was found by Mcllellan[20] in his retrospective study patients who went for open DPL for blunt abdominal injury revealed serious abdominal injury in 83% of cases. DPL with counts in the inconclusive range, 23% demonstrated serious injury with counts in the range of 0 to <20,000 cells/cumm, 67 per cent in the 20,000 to 50,000 range, and 86 per cent in the group above 50,000[21]. Occasionally one could perform repeat lavage after indeterminate results, which means infusing a second liter normal saline immediately if the initial return was faintly coloured. If the return was still weakly positive or darker, an exploratory laparotomy was performed. Accuracy of repeat lavage in 1-2 hours was 95.85%[22]. Repeat lavage could be offered to those patients who have indeterminate counts, who remain haemodynamically stable and who have persisting symptoms or signs suggestive of intraperitoneal injury. The timing of lavage will depend on the clinical findings. Secure fixation of the catheter to the abdominal wall under aseptic precautions when handling the catheter is most important to avoid misplacement and wound infection. However the advantages of DPL being that it is easily available, economical, fast, reliable bed-side investigation for ruling out intraperitoneal bleeding. While its oversensitiveness, lack of specificity, no information regarding extraperitoneal injuries, complications of injury to bladder or visceral organs, bowel perforation, hemorrhage, infection and subsequent incisional hernia are its recognized draw backs.

Ultrasound scanning. With the improvement in the portable equipment and rising experience, ultrasound scanning (US) has become an acceptable alternative to DPL, although there is concern regarding its sensitivity being operator dependant and its accuracy in comparison to CT in detecting and quantification of specific organ lesions. US is very accurate in detecting a haemoperitoneum with an overall sensitivity over 90%[23,24]. 250 ml of fluid detection by Ultrasound has been regarded as clinically significant indication for laparotomy[25] and 500ml of blood detected no more than 0 minutes after an accident as a strong indication for surgery. The indications for DPL also apply to US. The patient with haematuria and blunt thoracic injuries may also benefit from this investigation. The overall advantage of US is that being the least invasive investigation available. This can be done bed side in emergency room while patient is still under going assessment and resuscitation. In adults free peritoneal fluid of 70ml or more and in children smaller amounts can be detected. It is less time consuming and in about 4-15 minutes study is completed which includes examination of thorax and the retroperitoneum. Pleural and pericardial fluid can be easily identified in the same sitting. It can be used safely, economically without any hazardous effect on slightest suspicion of an intrabdominal injury or merely on a history of blunt trauma abdomen, even in uncooperative patients and in children.

US-Disadvantages: Although reports are considered operator dependent, interpretation errors occur when subcutaneous emphysema, gas distention or morbid obesity is present. The nature of fluid cannot be determined although US guided aspiration can overcome this difficulty[25,26]. In isolated bowel injuries diagnosis can be difficult in earlier stages as it takes time for collections to accumulate intraperitoneally[27]. Injuries to diaphragm, pancreas and large intraperitoneal haematomas may be difficult to assess with this technique. False negative and positive results may be obtained and may pose a problem considering that many injuries are not trivial and non therapeutic laparotomies carry the risk of morbidity[10]. Sensitivity, specificity and accuracy of US is reported as 91.7, 94.7 and 92.7 per cent respectively[27].

CT scanning has been used approximately for 15 years in the evaluation of intraabdominal injuries. Last decade has witnessed several major advances like non operative management of solid organ injury. This approach was on the basis of Karp et al[28] experience in blunt hepatic traumas using conservative approach on their belief that liver repair occurs in four stages

- A resorption of blood occurs over a period of two week period;
- B coalescence of lacerations
- C decease in size of the defect
- D virtually complete restoration of liver homogeneity at the end of a 3-4 month period

Critical objections to the non operative management at that time was based on the belief that:

- a blood in the peritoneal cavity, usually ascertained at that time by diagnosing peritoneal lavage, mandated celiotomy regardless of the haemodynamic status of the patient.
- b surgeons could not make rational decisions regarding an injury that could not be visually assessed with any degree of accuracy
- c most important concomitant intra abdominal injuries could not be detected with sufficient certainty to render non operation management safe[29]. With the advent of high speed advanced CT scan or helical scan most of the fears mentioned above have been allayed[30]. The CT scan delineates with a high degree of accuracy,
  - i the pathological anatomy
  - ii the severity of injury
  - iii assess and quantify the degree of haemoperitoneum
  - iv present highly reliable information regarding intraperitoneal and retroperitoneal injuries .Along with attributes of CT scanning came the recognition that anywhere between 20% to 67% of celiotomies for trauma are non therapeutic[28,31]. And 50% to 86 %of hepatic injuries have already stopped bleeding at the time of celiotomy[32,33]. CT scan allows subjective estimation and grading of the extent of haemoperitoneum. Quantification of blood in peritoneal cavity on CT scan is based on collections in seven intraperitoneal spaces with each space having the capacity to maintain a minimal volume of 125ml.[34] Collections are graded small (125-250ml) when limited to 1-2 spaces like perisplenic (left subphrenic) or perihepatic (right subphrenic) spaces, Morrisons pouch (hepatorenal fossa) or either the right or left paracolic gutter. Moderate collections (250-500ml) usually include two or more of these loculations in addition to the pelvis. Large collections (>500 ml) means collections in more than four spaces or in pelvis and other locations unless adhesion prevented free flow of blood[34,35]. Estimation based on accurate CT scan grading has made possible to manage Grade I-III liver injuries conservatively provided other criteria are met . CT scan is indicated in stable patients with no life threatening conditions equivocal abdominal examination, closed head injury, spinal cord injury, pelvic fracture with haematuria. CT scan can be accurate in 98.3% cases. Patients with minor injuries who don't require surgical intervention are reliably diagnosed and when decision to operate is based on CT scan findings, 86% laparotomies are therapeutic[36]. Helical CT has been major advancement in the evaluation of trauma patients because as scanning can be accomplished more quickly, with more intense bolus contrast material enhancement with combined studies of chest, abdomen, pelvis, head and extremities as required. Automated trauma protocols and rapid patient handling procedures have reduced patients' time for abdominal trauma CT to the 6-10 minutes range [37]. CT is less invasive than DPL. Sensitvity, specificity, accuracy rate for haemoperitoneum equals DPL. Haemoperitoneum of amount (> 100 ml) is accurately depicted. Specific organ injuries are reliably indicated whether intra or retroperitoneal. CT scan also shares disadvantages involving radiation hazards (the average radiation dose from one abdominal CT exam is 8.0 mSv, 400 times that of a ordinary chest radiograph[38]. The location of CT scan room may be such that transportation from emergency department may endanger patients life. Widespread variability in personnel and cooperation of patient is essential. Contrast reaction and with costly equipment are serious and important limitations. Patients who had both CT and US followed by DPL, the

sensitivity, specificity, and accuracy were respectively 97.2, 94.7, and 96.4 percent for CT, 91.7, 94.7 and 92.7 per cent for US, and 100, 84.2 and 94.5 percent for DPL[27].

LAPAROSCOPY: With the revival of interest in video assisted laproscopy there has been renewal of interest for use of this modality in blunt abdominal trauma patients who have equivocal findings and can select out those who have stopped bleeding or who may be treated laparoscopically. Haemoperitoneum can be divided into 4 categories, (no hemoperitoneum, minimal hemoperitoneum, moderate hemoperitoneum and severe hemoperitoneum). No hemoperitoneum means no blood is seen after thorough examination and a clear return after irrigating and suctioning. Minimal hemopritoneum is in a patient with a small volume of blood seen in the paracolic gutters or streaking on the loops of intestine. If after irrigation and aspiration there is no further blood noted, the patient may be observed and laparotomy avoided. Moderate hemoperitoneum is when there is a puddle of blood in the paracolic gutters and once aspirated, it returns. The source of bleeding can be localized laparoscopically and either coagulated if on the liver surface or sutured if a mesenteric bleed is found. If there is a brisk bleeding, then immediate laparotomy is indicated. Severe hemoperitoneum is when there is frank blood aspirated from the Veress needle, or the intestines are seen to be floating in a pool of blood and therefore, emergent laparotomy is indicated[39]. Though still in experimental stage, with a predictive vaue of 92 % versus DPL[40] unrecognized injuries to retroperitoneal structures and hollow organs are serious limitations, of laparoscopy, but needs further trials.

Conclusion

A In the literature there is consensus about the unreliability of initial abdominal examination following acute abdominal trauma. Olsen et al[7] reported misleading clinical findings in 45 percent of their cases. Rothlin et al[24] found abnormal clinical findings in 20 percent of patients with blunt abdominal or thoracic trauma. There is complex and extensive literature for use of diagnostic modalities in the management of blunt trauma abdomen. To avoid non therapeutic laparotomies and for non operative management despite proponents of each modality, there is now better understanding between emergency physician, surgeon and radiologist. In view of the potential for high doses of x-rays, CT examination should only be carried out if there has been proper clinical justification for the examination of each individual patient by an experienced radiologist. When clinically appropriate the alternative use of safer, non-ionizing technique such as US should be considered. Abdominal ultrasound is very reliable first step in the radiological assessment of blunt abdominal trauma patients, particularly in answering the question of whether emergency laparotomy is indicated because of intra abdominal bleeding[41]. Abdominal ultrasound should be considered as the "gold standard" in early evaluation of blunt abdominal trauma.

B For the appropriate management of severe trauma patients, role of Radiologist as a member of trauma team is essential.

C The trend towards conservative non operative management of bleeding low grade injures is rising if ICU, blood transfusion departments, and operating theatre facilities and expertise to intervene any time is available.

D Modern diagnostic imaging facilities have decreased the rate of non-therapeutic celiotomies.

E Despite being oversensitive and invasive and serious limitation in defining pathological anatomy DPL is rapid bed side simple modality to gain information.

F US/CT scan can detect small amounts and determination of amount of blood, and pathological anatomy are clear advantages.

G Accuracy and early assessment is now preferred to repeat clinical examination where expertise and appropriate facilities are available.

H The potential of keeping US in emergency room and inclusion of US training in surgical residency program is great.

I Guidelines regarding use of paracentesis, DPL, US, CT scan and Laparoscopy has to be available in emergency room.

J To improve the care of surgical patients, trauma has to be recognized as surgical disease as has been done by American college of Surgeons committee on trauma to establish standard care for trauma patients and organizing ATLS (advanced trauma life support)courses regularly for uniform thinking and action.

References:

1. Fischer RB and Dearsden CH. Improving the care of patients with major trauma in the Accident and Emergency department. Br Med J 1990; 300: 1560.
2. Stocchetti N, Pagliarini G, Gennari M et al . Trauma care in Italy; evidence of in-hospital preventable deaths. JTrauma 1994 ;36:401.
3. Rebecca Aft,Bowling W et al. Trauma In The Washington

manual of surgery/Department of Surgery , Washington school of Medicine , St. Louis, Missouri ; Gerad M Doherty. 1997; 372.

4. Donovan A J. Trauma Surgery. Techniques in Thoracic, abdominal and vascular surgery . Ist ed. Mosby year book , St. louis ,Missouri 1994 ;15.
5. Rodriguez A, DuPriest RW et al. Recognition of Intra-abdominal Injury in blunt trauma victims. Am Surg 1982; 48: 456.
6. Baker WN, Mackie DB et al. Diagnostic paracentesis in the acute abdomen. Br Med J 1967;iii:146.
7. Olsen WR, and Hildreth DH. Abdominal paracentesis and peritoneal lavage. J Trauma 1971: 11: 824.
8. Giacobine JW and Siler VE. Evaluation of diagnostic abdominal parcentesis with experimental and clinical studies. Surg GynecolObstet 1960; 110: 676.
9. Root HD, Hauser CW., et al. Diagnostic peritoneal lavage. Surgery 1965; 57;:633.
10. Chiquito PE..Blunt abdominal injuries. Diagnostic peritoneal lavage, ultrasonography, and computed tomography scanning.Injury 1996;27 :117.
11. Ochsner MG, Herr D et al. A modified seldinger technique for peritoneal lavage in trauma patients who are obese. Surg Gynecol Obstet 1991; 173: 158.
12. Cochran W, Sobat WS. Open versus closed diagnostic peritoneal lavage. A multiphasic prospective randomized comparison. Ann Surg 1984; 200:24.
13. Bivins BA, Jona JZ and Belin RP. Diagnostic peritoneal lavage in pediatric trauma. J Trauma 1976 : 16: 739.
14. Fischer RP, Beverlin BC, Engrav LH et al. Diagnostic peritoneal lavage. Fourteen years and 2586 patients later. Am J Surg 1978; 136: 701.
15. Gomez GA,Alvarez R,Plasencia G et al. Diagnostic peritoneal lavage in the management of blunt abdominal trauma a reassessment J Trauma 1987 ; 27:1
16. Bivins BA, Sachatello CR ,Daughtery ME et al. Diagnostic peritoneal lavage is superior to clinical evaluation in blunt abdominal trauma. Am Surg 1978 ;673.
17. Jaffin JH, Ochsner MG, Cole F J et al. Alkaline phosphatase levels in diagnostic peritoneal lavage fluid as predictor of hollow visceral injury. J Trauma 1994; 34 :829.
18. Jacobs DG, Angus L , Rodriguez A et al. Peritoneal lavage white count; a reassessment. J Trauma 1990; 30: 607.
19. D,Amelio L F and Rhodes M. A reassessment of the peritoneal lavage leucocyte count in blunt abdominal trauma. J Trauma 1990; 30:1291.
20. McLellan BA, Hanna SS, Monotoya DR et al. Analysis of peritoneal lavage parameters in blunt abdominal trauma. J Trauma 1985; 25: 393.
21. Hornyak S W and Shaftan G W . Value of " inconclusive lavage" in abdominal trauma management. J Trauma 1979 ; 5: 329.
22. Alyono D and Perry J F. Significance of repeating diagnostic peritoneal lavage .Surgery 1982; 91: 656.
23. Tso P; Rodriguez A, Cooper C et al. Sonography in blunt abdominal trauma. J Trauma 1992; 33: 39.
24. Rothlin Ma, Naf R, Amgwerd M et al. Ultrasound in blunt abdominal and thoracic trauma. J Trauma 1993; 34 :488.
25. Golletti O, Ghiselli G, Lippolis PV et al. The role of ultrasonography in blunt abdominal trauma. Results in 250 cases J trauma 1994; 36: 178.
26. Glazer K, Tschmelitsch J, Klinger P etal. Ultrasonography in the management of blunt abdominal ad thoracic trauma. Arch Surg 1994; 129: 743.
27. Liu M, Lee C-H and P,eng F-K. Prospective comparison of diagnostic peritoneal lavage, computed tomographic scanning, and ultrasonography for the diagnosis of blunt abdominal trauma J Trauma 1993; 35 : 267.
28. Karp MP, Cooney DR, Pros GA , et al. The non operative management of pediatric hepatic trauma. J Pediatr Surg. 1983; 18: 512.
29. Pachter HL, and Hofstetter SR. The current status of non operative management of adult blunt hepatic injurues. Am J Surg 1995 ; 169: 442 .
30. Mirvis SE, Whitely NO, Vainright JR , et al. Blunt hepatic trauma in adults . CT based classification and correlation with prognosis and treatment.Radiology .1989; 171 : 27.
31. Hollands MJ, Little JM. Non operative mangement of blunt liver injuies. Br J Surg. 1991; 78 : 968.
32. Cywes BS, Rode H, Millar AJW. Blunt liver trauma in children; non operative management. J Pediatr Surg . 1983; 18: 512.
33. Anderson R, Alwmark A, Gullstrand P, et al. Non operative treatment of blunt trauma to the liver and spleen. Acta Chir scand 1986; 152 : 739.
34. Federle MP, Jeffrey RB. Hemoperitoneum studied by computed tomography. Radiology . 1983; 148: 187.
35. Knudson MM, Lim RC, Oakes DD, Jeffrey RB, Jr. Non operative management of blunt liver injuries: the need for continued surveillance. J Trauma. 1990; 30: 1454.
36. Peitzmen AB, Makaroun MS, Slasky BS et al. Prospective study of computed tomography in initial management of blunt abdominal trauma. J Trauma 1986; 26: 585.
37. Shuman PW. CT of blunt abdominal trauma in adults. Radiology 1997; 205: 297.
38. Lindsell D. Imaging guidelines in Oxford textbook of Surgery, Morris P, Malt R oxford Medical Publications, Northants. UK. 1994; 1:298
39. Berci G, Sackier J, Paz-Partlow M. Emergency Laparoscopy. Am J Surg 1991; 161 : 332.
40. Sosa J, Sims D et al. Laproscopic evaluation of tangential abdominal gun shotwounds. Arch Surg 1992; 127:109.
41. Schurink GWH, Bode PJ, Van Luijt PA et al. The value of physical examination in the diagnosis of patients with blunt abdominal trauma: a retrospective study. Injury 1997; 28:261

Effects of Exposure to Cold and Exercise on Bronchial Asthma

Parvaiz Ahmad Koul; MD, Sunil Munshi; MD; DNB; MRCP

Humans generally insulate their bodies upon exposure to cold environment but the respiratory system is in direct contact with cold air and is, as such, affected by cooling of airways or via a variety of neural and hormonal responses of cooling of other structures (skin, CNS, etc.). A multitude of influences occurs upon respiratory mechanics,pulmonary circulation and ventilatory functions[1-12]. While these factors do have an influence on respiratory physiology in normal individuals, disorders of the respiratory system are also affected in a variety of ways.

Morphology of the respiratory tract and cold exposure

Cold exposure can be either intermittent or long term. Whereas short term exposure to cold may cause short term clinical effects, no morphological changes are effected. Tracheitis, excessive mucus production and focal destruction of superficial epithelium were demonstrated upon delivery of cold air (-50 to -28°C) to larynx ofanesthetized dogs. However, the effects were reversible within 48 hours[2]. Long term exposure to cold effects morphological changes in various parts of the respiratory tract[3,4]. These include:

a Trachea and large bronchi: Congestion with increase in goblet cells and mucus glands.
b Bronchioles and respiratory bronchioles: Hypertrophy of muscular facicles and thickening of basal collagenous membranes.
c Alveoli: Enlargement and thickening of alveolar-capillary interface.

Pulmonary vessels also demonstrate some changes upon long term exposure to cold and increase in muscle layer of terminal arteries and arterioles, increase in caliber of capillaries with protusion of capillaries into alveolar lumen and a general increase in lung vacular resistance-factors that may contribute to an increased prevalence of pulmonary hypertension in residents of cold areas[3,4].

Physiologically, cooling of the airways results in decrease of minuteventilation (VE)and sensitivityof ventilation to different chemical stimuli. Whereas laryngeal cooling has been shown to inhibit ventilation in new born animals and guinea pigs[5,6], the direct effects of cooling of the airways have been variably reported and are still under debate[1]. Some investigators have reported relaxing of the smooth muscle in humans[7,8],even as others have reported an increase in baseline tension and response to several agents like methacholine,acetyl choline and carbachol[9,10].

A decrease in airway mucosal blood flow has been shown to occur with cooling and/ordrying of the airways in laboratory animals. Bronchial vessels are also assumed to constrict upon cooling. Following cooling airway narrowing leads to reactive hyperemia of bronchial circulation resulting in congestion and edema which facilitates bronchoconstriction[11]. However, the response of the pulmonary circulation to direct cooling is bronchial vasodilatation[12]. The difference in response under the two conditions is due to a different avenue for cooling concomitant airway drying that occurs with cooling of air ways.

Cold/Exercise and Bronchial Asthma

Exercise and cold-induced asthma are commonly recognized respiratory disorders. Asthmatics are characterized by excessive airway narrowing (bronchial hyperreactivity) in response to antigenic as well as nonantigenic (i.e., exercise or voluntary hyperpnea in cold, dry air) stimuli. The antigenic and nonantigenic responses have different mechanisms and are synergistic. The bronchoconstrictor response to hyperventilation was first described about 50 years ago by Herxheimer[13]. In the early 1960's, Jones[14] reported that exercise increased airways resistance in asthmatic children. Presently, exercise-induced asthma is seen in 70-80% of clinically recognized asthmatics[15]. The incidence of reactions to exercise in cold air is similar in children and adults[15] and about 3-10% of otherwise asymptomatic athletes experience exercise-induced asthma[16]. Cold air

JK-Practitioner 1999; 6(1): 17-23

From the Department of Internal Medicine, SKIMS, Srinagar (Koul) **and Department of Medicine, Hospital Close, Evington Leicester, UK** (Munshi)

Received May 1998 Accepted December 1998

Correspondence to : Dr. Sunil Munshi, MD, DNB, MRCP (Edin) Senior Registrar, Department of Medicine, Hospital Close, Evington, Leicester, UK

hyperventilation and exercise are separate stimuli for bronchoconstriction that may act synergistically. There is also a group of otherwise asymptomatic patients in whom asthma occurs only in response to exercise and hyperpnea in cold air[16]. The asthmatic response includes several factors contributing to airway narrowing and increased airway resistance following exercise and/or voluntary isocapnic hyperpnea in cold air. These include airway smooth muscle contraction, mucus accumulation, decreased mucociliary clearance, bronchial vascular congestion, as well as epithelial damage and vascular leakage.

Generally, few symptoms occur during the period of exercise or cold, dry air hyperpnea itself. Rather, the effects are maximal within 5-15 min post-stimuli (early phase response). Studies in children[17,18] and adults[19-21] describe decreases in forced expiratory volume in one second (FEV_1), peak expiratory flow rate, maximum mid-expiratory flow rate, vital capacity, specific conductance, and increased residual volume[22]. Spontaneous recovery usually takes place within 30 minutes to 2 hours. There is usually a refractory period of about 1-2 hour during which responses to further stimuli are attenuated. A late phase response may occur 4-10 hours post-stimuli[22]. The severity of responses to both exercise and cold air stimuli depends on the temperature and water content of inspired air, level of ventilation, and hypersensitivity of airway smooth muscle. In the case of exercise-induced asthma in particular, exercise type, duration, intensity and interval between bouts are also important. Prior acclimatization to cold air has also been evidenced to attenuate the responses to cold air hyperpnea[22].

Diagnosis in patients with a positive history is accomplished with either an incremental maximal exercise test breathing temperate room air or voluntary hyperventilation of cold air at rest. FEV_1 is measured prechallenged and several times post challenge. A significant decrease in FEV_1 occurring 5-10 minutes post challenge leads to a positive diagnosis.

Pathogenesis:

Several stimuli have been proposed to initiate the increase in airway resistance following exercise or hyperpnea of cold, dry air. These include: a) airway cooling and/or drying; b) the isolated processes of exercise and/or hyperpnea themselves; or c) the humoral, neuromuscular or circulatory consequences of exercise of hyperpnea. The airway smooth muscle, mucus or blood flow responses to the above stimuli may be mediated through the following: a) direct influences; b) vagal reflexes triggered by airway sensory receptors; or c) responses to mediator release (Fig.1).

Symptoms of exercise-or cold-induced asthma generally do not occur during the stimuli period itself, rather the responses are delayed until 5-15 minutes post stimuli. Reasons for the delayed symptoms are unknown. However, since catecholamines and other agonists relax airway smooth muscle, the increase in plasma catecholamine levels during exercise may provide protection during and immediately post exercise until catecholamine levels return to baseline levels.

Early phase response:

The severity of the early phase symptoms is dependent upon the following:

a the thermal load placed on the airways (i.e., the level of ventilation, the temperature and water content of the inspirate, and the length of exposure)[23-27];

b the degree of non-specific hyperresponsiveness of the airways as measured by responses to histamine or methacholine[25-28];

c the intensity of the exercise itself[29]; and/or

d the degree and rapidity of airway rewarming following stimulation[11].

Airways cooling and drying

During inspiration, air is warmed and humidified as it passes along the conducting airways, resulting in airway cooling and hyperosmolarity of airway lining fluid. Both of these stimuli stimulate airway narrowing through bronchoconstruciton, mucus accumulation, and vascular engorgement (Fig.1).

Exercise

Whether or not exercise provides an isolated component to the response is still under debate. Some studies have shown that exercise-induced asthma cannot be explained entirely by heat or water loss[29-33]. For example, Noviski et al[32] varied exercise intensities while maintaining similar respiratory heat losses and demonstrated that, in asthamatic children, exercise intensity plays a role in determining the severity of symptoms. Other authors have also concluded that breathing cold air and exercise separately produce asthmatic effects and that these stimuli potentiate each other[29].

On the other hand, when experimental conditions have been controlled such that respiratory heat loss is similar with both voluntary and exercise hyperpnea, the same respiratory response (increase in airways resistance) was observed[34]. Exercise-induced asthma has also been completely inhibited when air at body temperature and water vapor was inhaled during

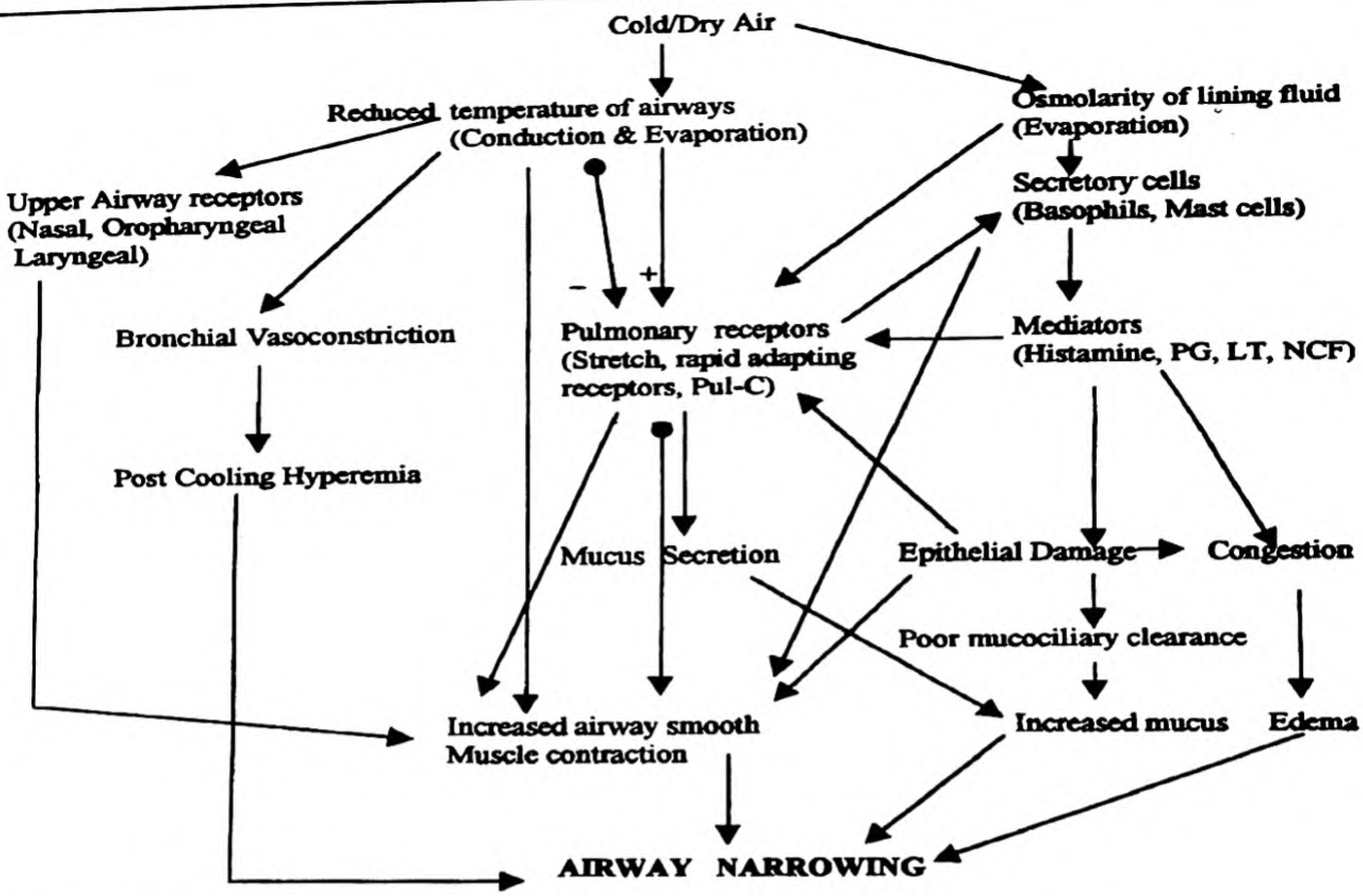

Cold/Dry Air
Reduced temperature of airways (Conduction & Evaporation)
Osmolarity of lining fluid (Evaporation)
Secretory cells (Basophils, Mast cells)
Upper Airway receptors (Nasal, Oropharyngeal Laryngeal)
-
+
Bronchial Vasoconstriction
Pulmonary receptors (Stretch, rapid adapting receptors, Pul-C)
Mediators (Histamine, PG, LT, NCF)
Post Cooling Hyperemia
Mucus Secretion
Epithelial Damage
Congestion
Poor mucociliary clearance
Increased airway smooth Muscle contraction
Increased mucus
Edema
AIRWAY NARROWING

Fig 1. Effects of cooling of airways on the respiratory system.
+ means a stimulatory effect and – an inhibitory effect. PG-prstaglandins, LT-Leukotrines, NCF Neutrophil chemotactic factor, Pul C – Pulmonbary C fibers.

exercise[35]. These latter results indicate that exercise itself is not a primary stimulus for bronchospasm.

Other factors

It is unlikely that other mechanisms such as hypocapnia[34], hyperpnea per se[34] or lactic acidosis[35] contribute in any significant way to the airway narrowing response to airway cooling. However, the conditions of post-stimuli rewarming have been shown to affect the bronchoconstrictive response to voluntry or exercise hyperpnea. McFadden et al[34] demonstrated that the response was greater when post-exercise conditions included warm vs. cold air, and if ventilation decreased quickly vs. slowly. These data indicate that the severity of responses are related to the rapidity and magnitude of post stimulus airway rewarming. Rewarming may have a direct effect on airway smooth muscle contractility; large contractions are seen in guinea pig tracheal muscle when cooling is followed by rapid rewarming[34]. It is also possible that rapid rewarming of bronchial vascular smooth muscle causes reactive hyperemia[34] resulting in luminal narrowing from vascular engorgement and edema[37,38]. This response could also be enhanced by the effect of released autocoids on vascular permeability[35].

Refractoriness

It has been demonstrated that airway obstruction declines in response to repetitive bouts of exercise within 1-2 f the initial bout[39-41]. Although the mechanisms are not clear, one explanation is depletion of histamine and other mediators from secretory cells during the early phase response[39,41-43]. O'Byrne and Jones[44] demonstrated that refractoriness to exercise is inhibited with indomethacin. This group further demonstrated that flurbiprofen, a prostaglandin synthetase inhibitor, attenuates leukotriene D_4 (LTD_4) tachyphylaxis and exercise refractoriness[45], indicating that exercise-induced prostaglandin release (which is mediated via the release of LTD_4) inhibits further contraction.

Late phase response

The existence of an exercise-related late phase response is controversial. In some patients airway resistance increases again 4-10 hours post stimulus. It is proposed that the late phase reaction must be preceded by, and the magnitude related to, an early response[46,47]. Mediators such as histamine, a high-molecular-weight neutrophil chemotactic factor and other arachidonic acid metabolites have been reported to increase in association with the delayed response[47,48]. This reaction does not occur in all patients, however, Zawadski et al[49] reported delayed responses in 7 of 20 patients following exercise breathing cold dry air. However, the delayed response in this group was similar to that following exercise, while breathing hot-humid air, or a methacholine challenge. These authors concluded that the delayed reaction was non-specific and was neither dependent on the existence of an early response nor was unique to exercise. Likewise, Karjalainen[50] observed delayed increases in airway resistance in only 9 of 404 symptomatic patients. This author felt the effect was an artifact consistent with spontaneous within day fluctuations in pulmonary function, pre-exercise bronchodilation, and airflow obstruction that persists long after the early post-exercise response.

Effects of Acclimatization

Observations indicate that trained asthmatics have less exercise-induced asthma that those who are untrained, and that in many individuals, symptoms are greater in early compared to late winter[51]. Haas et al[51] studied the effects of cold dry air inhalation and exercise before and after a series of exposures to cold air and found post-acclimatization bronchoconstriction to be less. Cold acclimatization of bare hands[52] and individual fingers[53] reduces cold-induced vasoconstriction, consequently increasing skin temperature. If bronchial vasculature responds likewise, acclimatization could have the effect of attenuating the decrease in airway temperature and bronchoconstrictive response to a given cold exposure. On the other hand, airway adaptation in the form of reduced mast cell release and/or receptor adaptation may also occur.

Physiologic Basis for Treatment and Prevention of cold induced asthma

When asthma attacks are primarily induced by exercise or cold, regular use of medication is usually unnecessary. The condition can usually be effectively controlled by use of medication prior to anticipated exposure as well as through some nonpharmacologic measures.

The standard and most effective single method of pharmacologic prevention is the use of an inhaled beta agonist 15-30 minutes prior to an exposure that the patient known from experience will trigger an attack[54,55]. Here, the bronchial changes that usually lead to an attack are not prevented but the final step, smooth muscle contraction, is attenuated through the direct action of the ß agonist on smooth muscle. When beta-agonists alone are not sufficient, inhalation of cromolyn sodium prior to exposure is added[55,56]. The exact mode of action of cromolyn is not yet well established, although mast cell membrane stabilization (leading to decreased mediator release) and inhibition of airway reflexes are suspected mechanisms.

In a minority of subjects the combination of a ß agonist and cromolyns not adequate to prevent attacks. In this case, other agents may be added. These include pre-exposure treatment with an inhaled anticholinergic agent (i.e., ipratropium bromide)[57], oral antihistamines (based on the likelihood that histamine release plays a major role)[58], a calcium channel blocker (i.e., nifedipine)[35] which acts mainly by blocking mast cell degranulation, or inhaled nedocromil (an anti-inflammatory agent).

Several new pharmacologic agents have recently shown promise for prevention of exercise-induced asthma. LTD_4 is released from airway mast cells during exercise and promotes airway smooth muscle contraction and increased bronchial vascular permeability[15]. Manning et al[45] demonstrated that intravenous LTD_4 receptor antagonist, attenuates the exercise-induced asthma response by 75%. Nasal provocation with cold, dry air also stimulates leukotriene release[59]. Other leukotriene antagonists have also been reported to attenuate 'old-induced broncho constriction[60]. PGE_2, a potent vasodilator, inhibits exercise-induced asthma[61]. The preventive effect was as great as with ß agonists, cromolyn or MK-571. These authors proposed that PGE_2 acts indirectly by blocking the release or increasing the washout of bronchoconstrictor mediators. Although this treatment is promising, the transient and refractory side effects of PGE_2 (cough and retrosternal soreness) must be dealt with before general use is possible. Finally, inhaled heparin indirectly inhibits exercise-induced asthma[62]. The proposed mechanism is modulation of mediator release rather than direct effects on airway smooth muscle. Heparin may bind to inositol triphosphate (ITP) receptors in mast cells to inhibit ITP-induced release of intracellular Ca^{++} or mast cell degranulation and histamine release.

In some subjects limiting the use of medication to prophylaxis prior to exposure is not sufficient. In such cases the regular use of medication is necessary. Inhaled corticosteroids and inhaled nedocromil are effective in reducing the inflammation usually present in these cases. At times, an initial course of oral corticosteroids is required to bring the inflammatiion under control.

Nonpharmacologic approaches are also useful and often reduce the need for medication. These include the following: 1) a 15-29 minutes warm-up (i.e., submaximal exercise) prior to the vigorous exercise is often protective: The intent here is to produce a mild degree of exercise induced asthma which would protect the subject from a more severe attack during the heavier bout. If the warm-up results in symptoms, pre-warm up use of a β agonist and/or cromolyn is usually effective. 2) Use of face masks: By causing the subject to rebreathe some of the humidified heated expired air, the physical conditioning which reduces the likelihood of attacks. 4) Avoidance of exercise in contaminated environments is recommended, because the presence of smoke and other irritants in the environment increase the risk and severity of attacks. Conversely, warm, humid environments are protective.

Conclusion

Cold exposure elicits several effects on the respiratory system. Pulmonary mechanics are worsened due to bronchoconstriction, airway congestion, secretions and decreased mucociliary clearance. The stimulus for these effects is likely a combination of direct airway cooling and hyperosmolarity of airway lining fluid when breathing cold dry air. These responses, which typically occur in exercise-or-cold-induced asthma, are mediated neurohumorally through reflexes initiated by vaguls rapidly adapting receptors and pulmonary strech receptors in the lower airways as well as thermosensitive receptors in the nasal cavity, oropharynx, larynx, face and trunk. There is a possible direct effect of cooling on airway smooth muscle. The exercise stimulus itself may also elicit part of the reflex responses.

The isolated ventilatory effects of cooling the airways are decreased baseline ventilation and ventilatory responses to chemical stimuli. However, these effects are small and unlikely to compromise acid-base homeostasis. In animals that use the respiratory system for thermoregulation, a decrease in ambient temperature elicits a change in breathing pattern favouring increased tidal volume and decreased deadspace ventilation, thus minimizing respiratory heat loss. Similar responses have not been documented in humans, however. Significant and rapid skin cooling can stimulate an acute gasp reflex and steady state alveolar hyperventilation. Subsequent hypocapnia-induced vasoconstriction of cerebral vessels may cause clouded mental function or syncopal episodes. The effects of central cooling are bi-directional. At moderately cool to normal core temperatures, ventilation follows the centrally and peripherally mediated increase in thermoregulatory heat production. However, at lower core temperatures the primary effect of cooling becomes evident: decreased tissue basal metabolism, relative hypoventilation and respiratory acidosis.

Cold exposure also elicits an increase in pulmonary vascular resistance. This stimulus is synergistic with hypoxia in mediating pulmonary hypertension and edema. Chronic exposure to cold environments results in morphological changes such as increased numbers of goblet cells and mucous glands, hypertrophy of airway muscular fascicles and increased muscle layer of terminal arteries and arterioles. Together, these latter factors may play a role in the symptoms of chronic obstructive pulmonary disease and bronchitis, high altitude pulmonary hypertension and edema, and right heart hypertrophy.

References:

1. Giesbrecht GG. The respiratory system in cold environment. Aviation Space Environ Med 1995; 66: 890-902.
2. Moritz AR, Weisiger Jr. Effects of cold air on the air passages and lungs; an experimental investigation. Arch Intern Med 1945; 75: 223-40.
3. Lutsenko MT, Tseluko NP, Krasavina NP. Peculiarities in morphology changes of respiratory organs during low temperatures influence in: Scientific abstracts and technical progress and Circumpolar health: The abstracts accepted for the IV International Symposium on Circumpolar Health, Novosibirsk, USSR, Oct. 2-7, 1978. Novobirsk: the USSR Academy of medical Sciences Siberian Branch, 1978: 105.
4. Marachev AG, Matveev LN. Morpho-functional manifestations of the respiratory tract adaptation in north inhabitants. In: Scientific abstracts and technical progress and Circumpolar health: The abstracts accepted for the IV International Symposium on Circumpular Health, Novosibirsk, USSR, Oct. 2-7, 1978. Novobirsk: the USSR Academy of medical Sciences Siberian Branch, 1978: 104.
5. Mathew OP, Anderson JW, Orani GP et al. Cooling mediates the ventilatory depression associated with airflow through the larynx. Resp Physiol 1990; 82: 359-68.
6. Motorola JP, Al-Shway S, Noworaj A. Importance of upper airway airflow in the ventilatory depression of laryngeal origin. pediatr Res 1983; 17: 550-2.
7. Badier M, Barthelemy P, Soler M, Jammes Y. In vivo and in vitro studies on cold induced airway response in normal and sensitized rabbits. Resp Physiol 1988; 73: 1-10.
8. Jongejan RC, De Jongste JC, Raatgeep RC, Bonya IL. Effect of cooling on responses of isolated human airways to pharmacologic and electrical stimulation. Am Rev Respir Dis 1991; 143: 369-74.
9. Bose D. Cold Induced contraction of canine airways smooth muscle. Fed Proc 1979; 38: 1545.
10. Bratton DL, Tanaka DT, Grunstein MM. Effects of temprature on cholinergic contractility of rabbit smooth muscle. J Appl Physiol 1987; 63: 1933-41.
11. McFadden ER Jr., Lenner KAM, Strhol KP. Postexertional airway rewarming and thermally induced asthma. New insights into pathophysiology and possible pathogenetic mechanisms.

Am Rev Respir Dis 1988; 73: 1-10.

12. Pisarri TE, Giesbrecht GG, Coleridge JCG, Colerige HM. Reflex tracheal smooth muscle contraction and bronchial vasodilation evoked by cooling the pumonary blood in dogs. FASEB J 1993; 7: A401.
13. Herxheimer H. Hyperventilation asthma. Lancet 1946; i: 83-7.
14. Jones RS, Wharton MJ, Buston MH. The place of physical exercise and bronchodilator durgs in the assement of the asthmatic child. Arch Dis Chilh 1963; 38: 539-45.
15. Sterk PJ, Fabbri LM, Quanjer PH, et al. Airway responsiveness. Standardized challenge testing with pharmacological, physical and a sensitizing stimuli in adults. Eur Respr J. 1993; 6: 53-83.
16. Pierson WE, Voy RO. Exercise induced bronchospasm in winter sports In: Casey MJ, Foster C, ed. Winter Sports Medicine. philadelphia: FA Davis Company, 1990: 158-66.
17. Glades-sebaldt M, Mclaughin FJ, Levison H. Comaprison of cold air, ultrasonic mist, and methacholine inhalation as tests of bronchial reactivity in normal and asthmatic children. J Paediatr 1985; 107: 526-30.
18. McLaughlin FJ, Dozor AJ. Cold air inhalation challenge in the diagnosis of asthma in children. Pediatrics. 1983; 72: 503-9.
19. Berk JI, Lenner KA, Mcfadden Er Jr. Cold induced bronchoconstriction,: role of cutneous reflexes vs direct airway effects. J Appl Physiol 1987; 63: 659-64.
20. Deal Ec Jr., McFaddwan EWr Jr., Ingram RH, Jagger JJ. Airway responsiveness to cold air and hyperpnea innormal subjects and in those with hay fever and asthma. Amer Rev Respir Dis 1980; 121: 621-8.
21. Strauss RH Jr., McFadden EW Jr., Ingram RH, Deal EC Jr., Jagger JJ. Enhancement of exercise induced asthma by cold air. Engl J Med 1977; 297: 743-7.
22. Gundersen I. The significance of the climaate in upper respiratory tract infections in children. In: Scientific abstracts and technical progress and Circumpolar health: The abstracts accepted for the IV International Symposium on Circumpolar Health, Novosibirsk, USSR, Oct. 2-7,1978. Novobirsk: the USSR Academy of Medical Sciences Siberian Branch, 1978: 234.
23. Deal Ec Jr., McFadden EWr Jr., Ingram RH, Jaggar JJ. Hypernea and heat flux: initial reaction sequrnce in exerciser induced asthma. J Appl Physiol 1979; 46: 476-83.
24. Deal Ec Jr., McFaddfen EWr Jr., Ingram Rh, Strauss RH, Jaggar JJ. Role of respiratory heat exchange in production of exercise induced asthma. J Appl Physiol 1979; 46: 467-75.
25. Eggle4ston PA. A comparison of the asthmatic response to methacholine and exercise. J Allerg Clin Immunol 1979; 63: 104-10.
26. Strauss RH Jr., McFadden EW Jr., Ingram RH, Deal EC Jr., Jdagger JJ. Influence of heat and humudity on the airway obstruction induced by exercise in asthma. J Clin Invest 1978; 61: 433-40.
27. Suzuki S, Chonan T, Sasaki H, Takishima T. Time course of response in exercise induced bronchoconstriction. Ann allergy 1984; 53: 341-6.
28. Obryne PM, Ryan G, Morris M, et al. Asthma induced by cold air and its relation to nonspecific bronchial responsiveness to methacholine. Am Rev Respir Dis 1982; 125: 281-5.
29. Exchenbacher WL, Sheppard D. Respiratory heat loss is not the sole stimulus for bronchoconstriction induced by isocapnic hypernea with dry air. Am Rev Respir Dis 1985; 131: 894-901.
30. Chen WY, Horton DJ. Heat and water loss from the airways and exercise induced asthma. Respiration 1977; 34: 305-13.
31. Ben-Dov I, bar-Yishay E, Godfrey S. Exercise induced asthma without respiratory heat loss. Thorax 1982; 37: 630-1.
32. Noviski N, Bar-Yishay Egur I, Godfrey S. Exercise intensity determines and climatic conditions modify the severity of exercise induced asthma. Am Rev Respir Dis 1987; 136: 592-4.
33. Zebllos RJ Shuturman-Ellstein R, McNally JF Jr., Hirsch JE, Souhrada JF. The role of hyperventilation in exercise induced bronchoconstriction. Am Rev Resp Dis 1978; 118: 877-84.
34. Struss RH Jr., McFadden EW Jr., Ingram RH. A critical assesment of the roles of circulation hydrogen ion and lactate in production of exercise induced asthma. J Clin Invest 1977; 60: 658-64.
35. Mcfadden EW Jr., Stearns Dr, Ingram RH, Leith DE. Relative contributions of hypercarbia and hypernea as mechanisms in postexercise asthma. J dAppl Physiol 1977; 42:22-7.
36. Souhrada JF, Preseley D, Souharada M. mechanisms of the temprature effect on airway smoth muscle. Respir Physiol 1981; 44: 311-23.
37. Gilbert IA, Fouke JM, McFadden ER Jr. Heat and water fflux in the intrathoracic airways and exercise induced asthma. J Appl Physiol 1987; 63: 1681-91.
38. Gilbert IA, Fouke JM, McFadden ER Jr. Intra-airways thermodynamics during exercise and hyperventilation in asthmatics. J Appl Physiol 1988; 64: 2167-74.
39. Edmunds AT, Tooley M, Godfrey S. The refractory period after exercise induced asthma; its duration and relation to the severity of exercise. Am rev Respir Dis 1978; 117: 247-54.
40. Henriksen JM, Dahl R, Lundquist GR. Influence of relative humidity and repeated exercise on exercise induced bronchoconstriction. Allergy 1981; 36: 463-70.
41. Jahmes L, Facaine J, Sly RM. Effect of treadmill exercise on asthmatic children. J Allergy Clin Immunol 1976; 57: 408-16.
42. Schoeffel RE, Anderson SD, Gillam I, Lindsay DA. Multiple exerrcise and histamine challenge in asthmatic patients. Thorax 1980; 35: 164-70.
43. Wilson NM, Barrles PJ, Vickers H, Silverman M. Hyperventilation induced asthma: evidence for two mechanisms. Thorax 1982; 37: 657-62.
44. O'Bryne PM, Jones GI. The effect of indomethacin on exercise induced bronchoconstriction and refractoriness after exercise. Am Rev respir Dis 1986; 134: 69-72.
45. Manning PJ, Watson RM, O'Brynne PM. Exercise induced refractoriness in asthmatic subjects involves leukotrine and prostaglandin interdependent mechanisms. Am Rev Respir Dis 1993; 148; 950-4.
46. Illiopoulos O, Proud D, Norman PS, Lichtenstein LM, Kagey Sobotka A, Naclerio RM. Nasal challenge with cold, dry. air induces a late phase reaction. Am Rev Respir Dis 1988; 138: 400-5.
47. Lee TH, Nagakura T, Papegeorgiou N, Iikura Y, Kay AB. Exercise induced late asthmatic reactions with neutrophil chemotactic activity. N Engl J Med 1983; 308: 1502-5.
48. Nagakura T, Lee TH, Assoufi BK, Denison D, Newman-Taylor AJ, Kay AB. Neutrophil chemotactic factor in exercise and

hyperventilation induced asthma. Am Rev Reswpir Dis 1983; 128: 294-6.
49. Zawadski DK, Lenner LA, McFadden ERJ. Re-examination of the late asthmatic response to exercise. Am Rev Respir Dis 1988; 137: 837-41.
50. Karajalainen I. Exercise response in 404 young men with asthma: No evidence for a late asthmatic reaction. Thorax 1991; 46: 100-4.
51. Haas F, Levin N, Pasierki S, Bishop M, Axen K. Reduced hypernea induced bronchospasm following repeated cold air challenge. J Appl Physiol 1986; 61: 210-4.
52. Nelms JD, Soper DJG. Cold vasodialtion and cold acclimatization in the hands of British fish filleters. J Appl Physiol 1962; 17: 444-8.
53. Adams T, Smith RE. Effect of chronic local exposure on finger temprature responses. J Appl Physiol 1962; 17: 317-22.
54. Sly RM. Management of exercise induced asthma. Drug Therapy 1982; 12: 95-9.
55. Woolley M, Anderson SD, Qigley BM. Duration of protective effect of terbutaline sulphate and cromolyn sodium combination on exercise induced asthma. Chest 1990; 97: 39-45.
56. Tullett WM, Tan KM, Wall Rt, Patel KR. Dose response effect of sodium cromoglycate pressurized aerosol in exercise induced asthma. Thorax 1985; 40: 4'-4.
57. Thomson Nc, Patel KR, Kerr JW. Sodium cromoglycate and ipratropium bromide in exercise induced asthma. Thorax 1979; 33: 694-9.
58. Hartley JPR, Nogardy SG. Effect of an inhaled antihistamine on exercise-induced asthma. Thorax 1980-35: 675-9.
59. Togias AG, Naclerio RM, Peters SP, et al. Local generation of sulfidopeptide leukotreines upon nasal provocation with cold, dry air. Am Rev Respir Dis 1986; 133: 1133-7.
60. Isreal E, Juniper EF, Callaghan JT, et al. Effect of a leukotreine antagonist, LY 171883, on cold air induced bronchocostriction in asthmatics. Am Rev Respir Dis 1989; 140: 1348-53.
61. Melillo E, Woolley KL, Manning PJ, Watson RM, O'Bryne PM. Effect of inhaled PGE$_2$ on exercise induced bronchoconstriction in asthmatic subjects. Am J Respir Crit Care Med 1994; 149: 1138-41.
62. Ahmed T, Garriago J, Danta I. Preventing bronchoconstriction in exercise induced asthma with inhaled heparin. N Engl J MEd 1993; 309: 90-5.
63. Scharter EN, Lach E, lee M. The protective effect ofm a cold weather mask on exercise-induced asthma. Ann Allerg 1981; 46: 12-6.

With Best Compliments From

Nira Sons

Chinar Trust Building, Maulana Azad Road, Srinagar-190001

DISTRIBUTORS FOR:

- ☐ **Hoechst Marion Roussell Ltd.**
- ☐ **German Remedies Ltd.**
- ☐ **Fulford India Ltd.**
- ☐ **S.G. Pharmaceuticals Ltd.**
- ☐ **Group Pharmaceuticals Ltd.**
- ☐ **Wockhardt Ltd.**
- ☐ **Searle India Ltd.**
- ☐ **Sarabhai Chemicals Ltd.**
- ☐ **Raptakos, Brett & Co. Ltd.**

ANTI-CANCER DRUGS AND ANTI-RABIES VACCINE AVAILABLE

Evidence-Based Medicine:
Transferring evidence from research into practice: The role of clinical care research evidence in clinical decisions

Tanveer Mir MD, FACP.

> *There is within medicine, somewhere beneath the pessimism and discouragement resulting from the disarray of the health care system and its stupendous cost, an undercurrent of almost outrageous optimism about what may lie ahead for the treatment of human disease if only we can keep learning.*
> —Lewis Thomas[1]

If Lewis Thomas was concerned about the disarray and cost of the health care system when he made this statement in 1979, he would be timely dismayed today. If he felt outrageous optimism then about the value of continuing learning, surely his optimism would have been dampened with each passing year by the increasing volume of new knowledge and the push for doctors to do more administrative unprecedented public and private investment, biomedical research has never been more productive of clinically important evidence than it is now. How tragic it would be if we lost our optimism for learning and applying new knowledge to clinical care just when we most need that knowledge to offset the adverse effects of resource slashes that are being made to control the stupendous cost of health care.

Evidence-based health care is a movement initiated by a broad coalition of clinicians, researchers, educators, policy makers, and many others to accelerate and improve the application of evidence from sound clinical care research to clinical practice[2]. (Evidence-based medicine is a subset of evidence-based health care.) Evidence-based health care is new enough to be misunderstood (by practitioners who worry that it might be "cookbook" medicine or, conversely, that they have been doing it all along[3]) and potent enough to be abused (by administrators and corporate executives who value the balance sheet above patients and practitioners). In this series, we will portray a model for evidence-based medical care that depicts each of the necessary steps, from evidence to practice, and describes the resources that are available to assist with each step. These steps include getting the research evidence straight; developing clinical policies that seek the best match between research evidence and the clinical circumstances in which we must practice; and then applying the research evidence to individual patients in the right way, place, and time[4]. We begin the series with a definition of evidence-based medicine and a simple model for evidence-based decision-making.

Definition

Evidence-based medicine is the conscientious and judicious use of current best evidence from clinical care research in the management of individual patients[5].

This definition is evolving and will continue to be refined (nitpickers, please note!). The key terms conscientious, judicious use, and current best evidence from clinical care research call for high standards for practitioners of evidence-based medicine. Conscientious means that evidence is applied consistently to each patient for whom it is relevant. Judicious use calls for the incorporation of clinical expertise that blanaces the risks and benefits of diagnostic tests and alternative treatments for each patient and takes into account his or her unique clinical circumstances, including baseline risk and cookbook medicine ignore this part of the definition of the term. Finally, current best evidence from the full spectrum of studies of the care of patients ("critical appraisal") and to provide themselves with very quick access to dependable, up-to-date sources of information in which the link with research evidence is explicit and honest.

An important symbiosis exists between evidence from clinical care research and evidence from research into the basic nature of health disorders. Studies in the laboratory and preliminary investigations in humans from the foundation of our knowledge about clinical problems and provide the groundwork for most diagnostic procedures and clinical interventions. To determine whether these inventions and insights do more good than harm, however, systematic studies of their application in clinical settings are needed. Evidence-based medicine

JK-Practitioner 1999; 6(1): 24-27

From the Department of Medicine Nassau County Medical Center (Tanveer)

Received September 1998 Accepted December 1998

Correspondence to : Dr. Tanveer Mir MD, FACP. Associate Programme Director Nassau Country Medical Center 2201-Hempstead Turnkpike East-Meadow NY 11554.

focuses on these systemic studies simply because they represent the most advanced stages of testing to ascertain whether the innovations of basic science work, how well they work, and for whom they work when applied in the clinical setting. Thus, evidence-based medicine is not in competition with basic science; rather it depends on it and builds on it.

The simple model for clinical descions has 3 components that might bear on the management of the patient's problems: clinical expertise, patient preference for alternative forms of care, and clinical research evidence. We note from the outset that potentially more poweful decision-making models exist[6] but must report that these models currently lack practical application for most clinical decisions. If is important to note that clinical expertise and patient preferences may override the other components of the model for a given decision. For example, clinical expertise must prevail if the clinician decides that the patient is too frail to have a surgical procedure that is otherwise best for his condition, and the patient's preference will dominate when she declines a treatment that clinical circumstances and research evidence indicate is best for her condition.

Clinical expertise

Clinical expertise is needed to assess the patient's problem: what is wrong, how severe it is, what comorbid conditions exist, and so on. In professional training and beyond, we learn the basic mechanisms of disease and pathophysiology and acquire skills in history taking, physical examination, diagnostic testing, and prescribing treatment. We then hone these skills by accumulating clinical expertise through observing the correlates and consquences of our actions in dealing with many patients. Although some clinical decisions are so simple that they can be done at least as well by machines[7,8], many elements of clinical assessment and management require both the advanced knowledge that medical education provides and the expertise that comes with experience and cannot be replicated even by very sophisticated computer programs[9]. Evidence form research can help to perfect that expertise[10] but cannot do the examination, let alone sort through the welter of information, both quantitative and qualitative, that practitioners collect, even in the first few moments of the clinical encounter. Clinical expertise is the crucial element that separates evidence-based medicine from cookbook medicine and the mindless applications of rules and guidelines.

Patient preferences

Patients have always exercised their preferences for care by seeking second opinions, choosing alternative therapies, preparing advance directives, and adhering or not adhering to prescribed treatments[11]. (Clinicians should not be surprised at this self-reliance: We often direct our own care when we become ill, with both good and bad consequences!) Moreover, today's patients have greater access to clinical information than ever before, and some become more knowledgeable about their conditions than their practitioners. Although the patient's role in clinical decisions is usually not formalized and is sometimes overridden or ignored by practitioners, it is nevertheless an important preferences is recognized in the emerging discipline of evidence-based patient choice, an approach to decision-making that deserves its own discussion[12].

Evidence from clinical care research

Advances in clinical care in the past 30 years have been astonishing: A host of lethal or limiting acute and chronic conditions are now becoming avoidable or at least much more manageable, including many types of cancer and the complications of premature birth, hypertension, diabetes mellitus, myocardial infarction, congestive heart failure, and peptic ulcer. No credible commentators deny that sound evidence from research must be an integral part of clinical decision-making. But how well is sound evidence from research incorporated into clinical decisions in practice? Not nearly as well as might be hoped. It took more than a decade after the appearance of unassailable evidence on the life-sparing value of thrombolytic therapy in acute myocardial infarction for it to be broadly accepted[13], and many institutons are still struggling with implementation. Studies show that the treatments that petients receive often reflect what the practitioner remembers from formal training rather than on current best treatment[14,15], a fact the lends testimony to the ready admission of practitioners that they feel overwhelmed by the clinical literature[16]. The critical question surrounding evidence-based medincine is not whether research evidence should play a role in clinical decisions-of course it should. Rather, the questions is how to establish this role effectively and efficiently. The challenge of integrating individual clinical expertise with current best evidence from systematic research is complex series will describe how evidence-based medicine addreses the 3 challenges of getting the evidence straight, of developing clinical policies that fairly balance research evidence with the realities of clinical practice, and of applying these policies in the right way.

The Cochrane Collaboration

ACP Journal Club, 1994 May-June: 120: A-11

We live in exciting times in health care: rich in information, full of promise, blessed with powerful scientific methods, and beset with turmoil over which clinical and other health care maneuvers to provide and how to pay for them. The health of present and future generations depends, in important ways, on our collective ability to identify and apply the affordable maneuvers that do more good than harm. This issue contains several examples of attempts to identify such amneuvers, including a pair of high-quality overviews on the efficacy of selective decontamination of the digestive system (SDD) in patients requiring intenseive care.

There is a science to the art of intervening in the health of persons and populations. It has its basis in the successful quest for interventions that produce huge changes in the structure and function of cells, tissues, organs, and entire organisms, including humans and their societies.

After the awful discovery that some of these interventions, developed and applied with the best of intentions, did more harm than good, health scientists developed powerful research methods for determining the efficacy and effectiveness of health interventions, culminating in the randomized controlled trial. The randomized trail is now the acknowledged gold standard for deciding whether a preventive, screening, diagnostic, therapeutic, rehabilitative, or even educational or administrative interventions does more good than harm; the primacy of randomized trials in this journal.

Field by field, authoritarianism based on mere seniority is giving way to authoritativeness based on randomized trials. The commanding role of the randomized trials is seen in the striving of researchers to design them and granting bodies to support their execution, in the speed and prominence with which they appear in scientific journals and the lay press, in their incorporation into regulations of drug-licensing and other health care agencies, and in their currency at the bedisde, in the boardroom, and in the corridors of health care institutions everywhere.

Too often, however, the results of randomized trials are ingored in providing health care; helpful maneuvers often are omitted, and useless or even harmful interventions often are applied. The reasons for these failures are several, and important among them are the simple unawareness of trial results and the confusion that arises when several trials of th same maneuver provide individually inconclusive or conflicting results.

To overcome this failure to provide evidence-based health care, a rapidly growing cadre of health care providers, consumers, and scientists have come together to engage in the unselfish, collaborative enterprise of preparing, maintaining, and disseminating systematic, up-to-date reviews, by specialty, of all relevant randomized controlled trials of health care (and, when they are not available, reviews of the most reliable evidence from other sources, the Cochrane Collaboration.

On the basis of shared interests and expertise in specific health problems, members are forming themselves into collaborative groups (called health Problem Review Groups) that carry out exhaustive searches for all relevant trials, scrutinize these for their relevance and quality, assemble and analyze them, draw conclusions about how their net result should be applied in health care, and prepare structured reports for widespread dissemination to health care providers and planners. The emerging evidence in this field thus fulfilling another objective of the Coachrane Collaboration: the avoidance of unnecessary duplication of effort.

Despite this assistance, forming and working in a health Problem Review Group are not for the faint-of-heart. These endeavors require an ego that is satisfied by unselfish collaboration and group, rather than individual, recognition; a career-long commitment to the continuing, exhaustive retrieval and analysis of all relevant trials; enormous numbers of hours of individual and group effort; and the subservience of personal convictions to scientific evidence.

But the rewards are great. The opportunity to remain at the cutting edge of one's field is unparalleled. The fun and learning that accompany working with a worldwide group of like-minded colleagues are exceptional. And in what other endeavor can you multiply your individual effectiveness a million-fold and contribute to the preservation and restoration of the health of countless persons around the world, in your own and subsequent generations?

Evidence-Based Medicine

ACP Journal Club. 1991 Mar-April; 114: A-16.

An internist sees a 70-year-old man whose main problem is fatigue. The initial investigation reveals a hemoglobin of 90 g/L. The internist suspects iron deficiency anemia. How might she proceed?

The way of the past

When faced with this situation during her training jsut a few years earlier, the internist was told by the attending physician that one follows this path. If both results come back below the laboratory's lower limit of normal, she will make a diagnosis of iron deficiency anemia, and investigate and treat accordingly. If both results are above the laboratory's cut-off point, she will look for an alternative diagnosis. If the results of the tests conflict, she can proceed according to her own clinical instincts, ask a more senior colleague or local hematologist how the results should be interpreted, or consult a textbook.

The way of the future

The internist asks herself whether she knows the diagnositic properties of the tests she is considering ordering and realizes she does not. She turns to the microcomputer in her office, which has a modern and inexpensive software to link by telepone to MEDLINE. She conducts a quick, computerized literature search, using the indexing terms "iron deficiency anemia" and "sensitivity and specificity," and retrieves seven citations at a cost $0.79. When she surveys the titles, one appears directly relevant[1]. She faxed the citation to the library at the local hospital and picks up the article when she does rounds the next morning. She reviews the paper and finds that it meets criteria she has previously learned about validation a diagnostic test[2] and that the results are applicable to patients like hers.

The study shows that she should order a serum ferritin level, but not transferrin saturation, which is less poweful and adds no useful information. She also finds that her laboratory's normal range for the test is misleading. The internist estimates the pretest likelihood of iron deficiency and orders the test. When the result is available, she uses data from the article to determine the sensitivity and specificity associated with the serum ferritin value obtained, calculates the poet-test probability of iron deficiency, and then decides on further management.

Discussion

The way of the future described above depicts an important advance in the inclusion of new evidence into clinical practice. Clinicians were formerly taught to look to authority (whether a textbook, an expert lecturer, or a local senior physician) to resolve issues of patient management. Evidence-based medicine uses additional strategies, including quickly tracking down publication of studies that are directly relevant to the clinical problem, critically appraising these studies, and applying the results of the best studies to the clinical problem at hand. It may also involve applying the scientific method in determining the optimal management of the individual patient[3].

For the clinician, evidence-based medicine requires skills of literature retrieval, critical appraisal, and information systematic approaches to make decisions when direct evidence is not available. The primary purpose of ACP Journal Club is to help make evidence-based medicine more feasible for internists by extracting new, sound clinical evidence from the morass of the biomedical literature so that practitioners can get at it.

We strongly recommend that these principles be adapted and incorporated in modern-day teaching Medical Institutions. The introduction of World Wide Web (www) and its application for answering both simple and difficult queries in Medicine is of unique value and its utility cannot be underestimated. Our experience with EBM and tools like WWW has been extermely useful and is a commonly used tool in our Morning Report Conferences.

References:

1. Thomas L. The Medusa and the Snail. More Notes of a Biology Watcher. New York: Viking Press; 1979.
2. Evidence-Based Medicine Working Group. JAMA. 1992; 268: 2420-5.
3. Morgan WK. Lancet. 1995; 346: 1172.
4. Haynes RB, Hayward RS, Lomas J. J Am Med Inform Assoc. 1995; 2: 342-50.
5. Sackett DL, Rosenberg WMC, Gray JA, Haynes RB, Richardson WS. BMJ. 1996; 312: 71-2.
6. Dowie J. J Health Serv Res Policy. 19965; 1:104-13.
7. De Dombal FT, Leaper DJ, Horrocks JC, Staniland JR, McCann AP. Br Med J. 1974;1: 376-80.
8. Pozen MW, D' Agostino RB, Mitchell JB, et al. Ann Intern Med. 1980; 92L238-42.
9. Berner ES, Webster DG, Shugerman AA. N Engl J Med. 1994; 330: 1792-6.
10. Panzer R, Black E, Griner P. Diagnostic Strategies for Common Medical Problems. Philadelphia: American College of Physicians; 1991.
11. Haynes RB, Taylor DW, Sackett DL, eds. Compliance in Health Care. Baltimore: Johns Hopkins University Press: 1995.
12. Hope T. Report to the Anglia and Oxford Healh Authority into the use of evidence based information for enhancing patient choice. Old Road, Headington, Oxford: Anglia and Oxford Regional Health Authority; October 1995.
13. Antman EM, Lau J. Kupelnick B, Mosteller F, Chalmers TC. JAMA. 1992; 268: 240-8.
14. Anderson FA Jr, Wheeler HB, Goldgerg RJ. Ann Intern Med. 1991; 115: 591-5.
15. Evans CE, Haynes RB, Bilbert Jr, et al. Can Med Assoc J. 1984; 130: 719-22.
16. Williamson JW, German PS, Weiss R, Skinner EA, Bowes F3d. Ann Intern Med. 1989: 110: 151-60.
17. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical Epikemiology, a Basic Science for Clinical medicine. 2nd ed. Boston: Little, Brown and Company. (In Press for 1991).
18. Guyatt GH, Keller JL, Jaeschke R, et al. Then-of-1 randomized contolled trial: Clinical usefulness. Our three-year experience. Ann Intern Med. 1990; 112: 293-9.

Epidemic Dropsy in Jammu - Clinical Study and Review

Gazanfar Ali M.D.; Manoj Kumar M.D.; Bhagwan Dass M.D.; Anil Mahajan M.B.B.S.; Hishu Sharma M.B.B.S.; M.B.Wadhwa M.D.; Ashok Parihar M.D.

Abstract: *We report an out break of epidemic dropsy which occured in Jammu (J&K) in September 1998. This is the first report of this condition from J&K state. This outbreak in the state was part of the major epidemic which engulfed many parts of India in August 1998.*

Key words: *Epidemic dropsy, Argemone Oil, Sanguinecrine.*

JK-Practitioner 1999; 6(1): 28-31

Introduction

The cause of epidemic dropsy was not known until 1926 when Sarkar[1] ascribed it to the contamination of mustard oil with Argemone oil. Argemone seeds contain a toxic alkaloid "Sanguinerine" identified by Sarkar[1] and shown to produce widespread capillary dilatation and increased capillary permeability. It interferes with oxidation of pyruvic acid, and subconjunctival injection of this oil raises ocular tension in rabbits. Consumption of edible oil adulterated with argemone oil leading to eipidemic dropsy was proved subsequently by other investigators[2,3]. After the first report from Calcutta[4] in 1877, various reports have appeared from many parts of India. Patwardhan[5] in his book on "Nutrition in India" mentioned regarding epidemics in Mauritius (1879), Fiji Islands (1926), Rangoon & South Africa (1950). Awareness of this condition occuring in people consuming oils other than mustard oil was brought to light by various reports[6,7,8]. It was further stressed by Shah[9] and by Wadia et al[10].

Material and Methods:

This series includes eleven cases of epidemic dropsy. A detailed history with special stress on the type of oil consumed was recorded. Complete clinical and opthalmological examination including tonometery & fundus examination were carried out. Other investigations included complete haemogram, peripheral blood smear, routine urine examination, BUN studies and liver function tests in all the patients. Chest radiography and ECG were taken in all. Nitric acid test and chromatography for argemone oil contamination was done in all oil samples of the affected families (paper chromatography can detect argemone oil upto 0.0001 percent in all edible oils and fats). Skin biopsy of two patients was performed. Patients were followed for two weeks.

Results:

Age distribution of the patients in given in Table 1. The patients belonged to five families comming from different areas of Jammu region. The edible oil consumed by the patients of four families was mustard oil and one family was consuming refined vegetable oil. The socioeconomic status of three families was upper middle class and two families came from lower socioeconomic group. The clinical and laboratory data of the patients is summarized in Table 2 & Table 3 respectively.

Table 1
Age distribution of patients (n =11)

Age (Yrs.)	No of Cases
3-9	1
10-19	4
20-39	5
> 40	1
Total	**11**

Table 2
Clinical features of patients

S.No.	Clinical Features	No. of Cases	Percentage
1.	Oedema a) feet	11	100
	b) hands & thighs	4	36
2.	Persistent tachycardia	8	73
3.	Redness over oedematous part with tenderness	4	36
4.	Diarrhoea	11	100
5.	Vomiting	8	73
6.	Fever	2	18
7.	Raised JVP	3	27
8.	Collapsing pulse	2	18
9.	Tender hepatomegaly	5	45
10.	Dyspnoea	3	27
11.	Cardiomegaly	3	27
12.	Gallop rhythm	1	9
13.	Papilloedema	0	0
14.	Glaucoma	0	0
15.	Absent jerks	0	0
16.	Skin changes	4	36

From the Department of Medicine, Govt. Medical College Jammu (J&K) India (Ali, Manoj, Dass, Mahajan, Sharma, Wadhwa, Prof. Parihar)

Received November 1998 Accepted December 1998

Correspondance to : Dr Gazanfar Ali, M-5 Wazarat Road, Jammu (India)

Table 3
Reports of investigations of patients

S.No.	Investigation	No. of Cases	Result
1.	Haemogram		
	Hb percent	8	> 10 gms.
		3	8-10 gms.
	TLC	11	range 5000-10500 cu.mm
	DLC	11	normal
	ESR	8	>25 mm
	(1st hr. westergren)	3	<15 mm
2.	Urine examination including 24 hr. urinary protein	11	normal
3.	BUN	11	normal
4.	ECG	11	Sinus tachycardia (11) T wave inversion (3)
5.	Chest X-ray	11	CT ration > 55 (3)
6.	Ultrasound Abdomen	11	Hepatomegaly (4)
7.	Skin biopsy	2	Loss of rete pegs, dialation and proliferation of capillaries

Discussion:

Epidemic dropsy occurs after ingestion of edible oil contaminated by argemone mexicana; however, it can also follow the ingestion of wheat mixed with argemone seeds as occured in an epidemic in South Africa[11]. It is characterized by gastrointestinal disturbances, oedema of feet & legs, vascular changes and cardiac insufficiency.

The youngest patient in our series was 8 years old. In various reports by Thakur and Prasad[12], Shah et al[7] and Wadia et al[10], the youngest patient was 2.5 years, 5 years and 3 years respectively. Children below the age of two years, and those nourished mainly on milk and breast fed babies in the affected families are spared[10]. Though, the toxic alkaloid "Sanguinerine hydrochloride" has been proved to be present in the breast milk[13], the exclusion of breastfed babies is probably due to a low concentration of this alkaloid. In the present study none of patients had consumed oils other than mustard oil, which can also get contaminated and produce epidemic dropsy[6-8, 14,15]. The contamination of mustard or other oils may be accidental or deliberate. Seeds of argemone mexicana (prickly poppy) closely resemble mustard seeds. The plant grows in India. It has prickly leaves and bright yellow flowers. Crops of mustard are gathered during March and during this period seeds of argemone also mature and are lilely to be harvested along with mustard seeds. Some times unscrupulous dealers mix argemone oil with mustard and other edible oils.

The study of the family distribution of the affected cases in this series revealed that 12 persons were spared. The appearent escape of these persons can not be explained except in one family where the unaffected member was a child of 7 years who was not taking any fried food. It could be argued that the unaffected members had consumed very little of contaiminated oil[15], or the tolerability of an individual to a particular concentration of argemone oil could vary. The most striking clinical feature seen in our cases was the rapid appearance of oedema in all as has been reported in the earlier epidemics[9,10,12,15]. Tenderness and erythema over oedematous part was seen in 36 percent of the cases as compared to 75 percent reported by Sainani et al[15]. Review of literature reveals that the clinical features vary slightly from epidemic to epidemic. The remarkable symptom of severe burning feet with paraesthesias reported earlier in majority of patients[15], was not observed by us. This symptom was also not reported by others[6,9,12,16]. Wadia et al[10] & Shanbhag et al[14] in long term follow up noted that oedema may last for many weeks. In the present outbreak diarrhoea preceded oedema in 100 percent of cases as in Purulia[17] and Chandrapur[15] epidemics. Fever was present in 18 percent of our patients while Sainani et al[15] reported it in 41 percent and Wadia et al[10] in 30 percent of cases. Most of the epidemics[10,12,14] have not reported vomiting as a symptom of epidemic dropsy but we observed this in 73 percent of patients as also reported earlier in one series[11]. Cardiac involvement of varying degrees has been described in previous epidemics[17,18] & in experiments[19]. Affection of cardiovascular system in the leading cause of death. Detailed study of the cardiovascular manifestations of epidemic dropsy and their treatment has been described by Chopra and Basu.[20] We observed frank congestive cardiac failure in 3 cases (27 percent) where as Sainani et al[15] reported it in 8.8 percent. Thakur et al[12] in 5.3 percent, Shah et al[7] in 4 percent and Wadia et al[10] in 5.4 percent of cases. ECG changes include shortened PR interval[20], sinus tachycardia and T wave inversion[5,9,10]. In our series the abnormalities noted were sinus tachycarida in 100 percent, T wave inversion from V1-V4 in 18 percent as also reported earlier[15]. Three of our patients who had congestive cardiac failure also had signs of hyperdynamic circulation. Chopra and Basu[20] observed severe heart failure in 25 percent cases where as the incidence reported in other epidemics vried from 4 percent[7], 4.8 percent[14], 5.3 percent[12], 5.4[10] to 8.8 percent[15].

Tender hepatomegaly was observed in 45 percent of our cases, where as definite signs of congestive cardiac failure were present in only 27 percent. This compares well with Sainani et al[15]. It appears that some other mechanism is operative for hepatic enlargement[5]. Histologically various hepatic changes like portal congestion, thrombosis of portal vein tributaries, fatty degeneration of liver cells and occasional necrotic patches have been described[5].

Eye changes like early venous congestion[9] on fundoscopy and papilloedema[5] have been described in epidemic dropsy. Glaucoma which occurs in these patients[11,17,21] was not seen in any of our patients Glaucoma was reported in 10 out of 119 patients seen in Guru Nanak Eye centre in New Delhi by 4th September 1998[22]. Many earlier studies have not reported glaucoma in their series[6,10,14,15].

Anaemia occurs in many of the patients[15,23,24]. However it was present in only 27 percent of our cases. It is supposed to be due to bone marrow depression or partly because the patients involved in epidemic dropsy belong to lower socioeconomic group[15] ESR is raised almost in all patients[12,15,23,25]. 73 percent patients in this study had raised ESR. Blood chemistry such as blood sugar, urea, serum creatinine, cholesterol, uric acid & electrolytes have been found to be normal in epidemic dropsy[9,14]. Routine urine examination was normal in all our cases as also reported previously[14,15]. The clinical findings and laboratory investigations reveal that oedema of the epidemic dropsy is not due to cardiac, hepatic or renal disease. The oedema is a result of increased capillary permeability[7,10,26] whereby albumin drains out into extracellular space reducing intravascular osmotic presure while blood viscosity is also lowered. However marked disturbances of electrolyte balance has been reported to be the cause of oedema in some cases[27,28] Histopathology of skin in two patients showed flattening of rate pegs and dilatation and proliferation of capillaries in the dermis with presence of a few lymphocytes and monouclear cells around the capillaries. This finding has also been demonstrated in 5 cases by Shah et al[7] and Wadia et al[10].

The prognosis in epidemic dropsy is guarded and depends chiefly on cardiac state. The main cause of death is severe heart failure. The mortality rate is usually around 5 percent[19,15]. None of our patients died. In the 1998 epidemic of argemone poisoning in India approximately 60 patients died in New Delhi only.

Follow up studies of patients have shown that some manifestations may last for 8 to 10 weeks[14]. Wadia et al[11] in their one year of follow up of cases reported that 25 percent of patients remained symptomatic for 2 months (oedema) & 10 percent for more than 5 months. We followed our patients for 8 weeks and found only one patient persisting with mild pedal oedema while the rest were asymptomatic.

The treatment of epidemic dropsy is symptomatic. Salt free, protein rich diet and diuretics constitute the basic therapeutic regimen[16]. Careful watch has to be kept on heart and eyes. Review of literature revealed many therapies like Vit C, E and Phenergan, but they have no specific therapeutic effect[14,16]. Shah et al[6,7] treated 59 seriously ill patients with corticosteroids. The dropsy and other symptoms disappeared in 47 patients. In 1998 epidemic in India beneficial effects of steroids were reported from various institutes of India (quoted in national press in Sep. 1998). Preventive measures should from the most important aspect of treatment.

References:

1. Sarkar SN. Isolation from argemone oil dihydrosanguinerine and Sanguinerine toxicity. Nature 1948, 162: 265-267.
2. Sanyal PK. Argemone and the mustard seeds. Ind Med Gaz 1950; 85: 948-50.
3. Bhende YM. Vascular changes produced by argemone oil. II changes in rats given injection of the oil. J post Grad Med 1956; 2: 185-187.
4. Manson Bahr P. "Epidemi dropsy". Manson's Tropical diseases, 16th ed. Bailliere, Tindall & Cassell Ltd. London, 1966; p 745.
5. Patwardhan VN. Nutrition in India. Ist Ed, Published by Ind J Med SCI 1952. p 201.
6. Shah M J, Lewis R.A. Epidemic dropsy, Nadiad epidemic ____Observations on serum proteins and cartisone therapy. J Ind Med Asso 1955; 24: 245-248.
7. Shah MJ, Manghani KK, Seth PU. "Epidemic dropsy. Epidemiological, Clinical and therapeutic observation in 67 cases." Ind J Med Res. 1969; 57:P 1878-1891.
8. Deodhar NS. "Epidemic dropsy" In Poona 1969. Maharashtra Med J 1970; 17: 131-133.
9. Shah MJ. Epidemic dropsy as a social and medical problem. JAPI 1971, 19: 369-373.
10. Wadia RS; Relwani GS; Batra RK, Ichaporia RN; Grant KB. Epidemic dropsy in Poona, 1969 (Clinical features and one year follow UP) JAPI 1971; 19: 641-643.
11. Meaker RE. Argemone Mexicane seed posoning. South African MEd J 1951; 24: 331-333.
12. Jhakur CP; Prasad S. Observations on a recent outbreak of epidemic dropsy. J Ind Med Asso 1968, 50: 203-205.
13. Hakim S; Majovic V, Walker J. Distribution of certain poppyuu Fumaria alkaloid and a possible link with the incidence of Glucoma. Nature 1961; 189: 198-207.
14. Shanbagh VV; Jha SS, Kekre MS; Rindani CJ. Epidemic dropsy in Bombay City and Suburbs. Ind J Med Sci. 1968; 27: 226-228.
15. Sainani GS; RTajkandawar VL; Wechalekar MD; Wechalekar DK. Epidemic dropsy in Chandrapur (Maharashtra) JAPI 1972, 20: 301-306.
16. Chaudhari RN; Chakravarty NK. Treatment of epidemic dropsy. Ind Med Gaz 1950; 85: 165-172.
17. Chopra RN; pasricha CL; Banerjee K. Outbreak of epidemic dropsy. Ind Med Gaz 1940; 75: 261-263.
18. Desai RA; Mohile GB. Epidemic dropsy in Nadiad. J Ind Med Asso 1955; 24: 248-250.
19. Chakravarty NK, Chaudhari RN, Warner G. Observation on Vascular changes produced by argemone oil (alkaloids). Ind J Med Res 1955; 43: 107-108.
20. Chopra RN; Basu VP. Cardio Vascular manifestations of epidemic dropsy and their treatment. Ind Med Gaz 1930; 65: 546-548.

21. Chopra RN; Pasricha CL; Goyal RK; Lal RB; Sen AK. Experimental production of syndrome (epidemic dropsy). Ind Med Gaz 1939; 74: 193-194.
22. Ten cases of Glucoma. Reported in "The Pioneer" Sep. 5, 1998, p.3.
23. Sengupta PC; Napier LE. Haematological changes in epidemic dropsy. Ind J Med Res 1940; 28: 197-199.
24. Ray C. Epidemic dropsy, its blood picture, general and metabolic. Ind J Med Res 1927; 15: 67-69.
25. Pasricha CC; milik KS; Lal S. Sedimentation of red blood cells in epidemic dropsy. Ind Med Gaz 1941; 76: 34-37.
26. Bhende YM; Vasudeva NB; Gandhi NM. Epidemic dropsy (Nadiad epidemic Pathogenesis of edema. J post Grad MEd 1955; 1: 27-29.
27. Bhende YM. Epidemic dropsy-Vascular changes in argemone oil poisoning. J Post Grad Med 1995; 2: 125-127.
28. Hansen JDL; Brock JF. Potassium deficiency in the pathogenesis of nutritional edema in infants. Lancet 1954; 2: 477-478.

BM Scientific Company

GOLE MARKET, KARAN NAGAR, SRINAGAR - 10, KASHMIR

DISTRIBUTORS FOR:

- Borosil Glass Works Ltd., Bombay
- Gupta Scientific Industries, Amballa
- Elico Ltd., Hyderabad
- Loba Chemie Pvt. Ltd., Bombay
- Narang Scientific Works Pvt. Ltd., Delhi
- Sisco Research Laboratories Pvt. Ltd., Bombay
- Glaxo India Ltd., Bombay
- Whatman Ltd., UK
- S.D.Fine Chemicals, Bombay
- Ke-Roy Balances, Varanasi
- Dhona Instruments, Calcutta

Hydrocephalus in Children: Analysis of 50 Patients

Nasib C. Digray, MS, M.Ch.; Y. Mengi, MS, M.Ch.; H.L. Goswamy, MS, M.Ch.

Abstract: *Fifty patients of hydrocephalus, managed over a period of 5 years are analyzed. Most of the children were in the age group of 1 month to 1 year, with congenital hydrocephalus being the commonest cause. Significant number of patients also had associated meningocele or encephalocele. Cranial ultrasound was the most useful investigation for diagnosis. Ventriculoperitoneal shunt was the primary procedure done in all patients. Fifteen patients had shunt related complications, blocked shunts being the most common. Shunt revision was done on 10 occasions (6 patients) and one patient each underwent ventriculoatrial and ventriculo-cholecystic shunts.*

Key words: *Hydrocephalus, Meningocele, cerebrospinal fluid shunts, Spina bifida.*

JK-Practitioner 1999; 6(1): 32-34

Introduction

Hydrocephalus is a frequently encountered problem in infancy and is most commonly treated by placement of ventriculoperitoneal (VP) shunt or ventriculoatrial (VA) shunt. Other sites for the insertion of distal shunt end have included the stomach, ureter, pleural cavity and fallopian tubes. No shunt procedure is free from complication like infections and blockage of the shunt. Some of these patients may need multiple revisions or alternate shunt procedures like ventriculo-cholecystic (VC) shunt. We analyzed our experience in a series of 50 patients of hydrocephalus seen over a period of 5 years, which forms the basis of this study.

Patients and Methods

This study is based on 50 patients of hydrocephalus managed over a period of 5 years (Jan.' 1991 to Dec.' 1995) at the department of surgery, Government Medical College, Jammu. Majority of the patients were in the age group of 1 month to 1 year. Table 1 shows the distribution of these cases according to the age and etiology. Forty patients presented with incease in head size disproportionate to their age, while 5 cases were diagnosed on antenatal ultrasonography. Delayed milestones and features of raised intracranial pressure (ICP) were present in 10 and 5 cases respectively. Majority of the patients were diagnosed on cranial ultrasonography and only a few patients needed CT scan. A ventriculo-hemisphere ratio (VHR) more than 0.33 was taken to be suggestive of hydrocephalus. Skull x-rays were rarely used and preoperative CSF analysis was done only in those patients who had hydrocephalus following meningitis or subarachnoid haemorrhage (SAH). Only those patients who had normal CSF parameters including a protein content of > 100 mg% were taken up for surgery. All patients were started on antibiotics 12 hours before surgery and these were continued for 7 to 10 days postoperatively. VP shunt (MDR) was the primary procedure done in all the patients using Upadhya or Chhabra type shunt. Standard technique for insertion of shunt was followed. In some patients whole length of distal catheter was inserted into the peritoneal cavity. Two patients who needed multiple revisions were revised to VA shunt and VC shunt respectively. Peroperative CSF studies were done in all the patients. On follow up parameters like head circumference, anteriorr fontenellae, shunt patency and developmental milestones were recorded regularly. Ultrasonography/CT scan was done wherever necessary.

Table-1: Etiology of Hydrocephalus

Age	Congenital	MMC	Meningitis	SAH
< 1 month	7	2	—	1
1 month -1 yr.	14	8	2	—
1-3 yrs.	5	2	5	—
> 3 yrs.	—	—	4	—
Total (50)	26	12	11	1

Results

Fifty patients of hydrocephalus who underwent VP shunt as primary surgery are analysed. Most of the patients were infants diagnosed by cranial ultrasonography. Fifteen patients had shunt related complications during a follow up period of 6 years. Most of the complications occurred during first 3 months following VP shunts. Shunt Blockage was the commonest complication occuring in 9 patients. Of these blocked shunts 3 patients had spontaneous arrest of

From the Department of Surgery (Digray, Mengi, Goswamy) **Govt. Medical College Jammu, J&K, India**

Received June 1998 Accepted December 1998

Correspondence to : Nasib C. Digray, H.No. 220, Sarwal Colony, Jammu, J&K, India. 180005

hydrocephalus and didn't require any further treatment. Remaining 6 patients had revision of shunts on 10 occasions (1.6/patient) and 2 of these further required VA and VC shunts. Lower end of the shunts was blocked more commonly than the upper end. The causes of blockade being peritoneal pseudocyst, omental plugging, shortened peritoneal catheter and non-absorbing tense ascitis at the lower end and brain debris, blood/choroid plexus and protein exudate blocking the upper end. Skin necrosis of scalp overlying the shunt chamber and skin tract infection occured in 3 patients. In one of these patients the ventricular end was found extruding through the necrosed skin overlying the shunt chamber. This patient required shunt revision while other two patients settled with conservative treatment. Two patients had intestinal obstruction because of adhesions requiring laparotomy. One patient developed isolated facial nerve palsy following shunt and this responded to steroids. The various complications are shown in Table 2. It was found that etiology of hydrocephalus and length of peritoneal catheter didn't influence the out-come of the shunt procedure. Interestingly none of our patients had shunt infection necessitating shunt removal/revision. There was no mortality in our series.

Table-2: Complications of VP Shunt (n=15)

Complications	No. of Patients	Treatment
1. Infection	02	Conservative
2. Extrusion	01	Revision
3. Blockage	09	Revision : 6 Spontaneous arrest : 3
4. Intestinal Obst.	02	Lap. + Adhesiolysis
5. Facial N Plasy	01	Conservative
Total	15	

Discussion

Hydrocephalus is a common peadiatric problem and urgency of its management depends on etiology, age and clinical presentation of the patient. In majority of the children, the cause is congenital either due to aqueduct stenosis or Arnold Chiari malformation associated with spina bifida. Other causes are tumors, trauma and meningitis[1]. In most of the patients, the diagnosis is obvious clinically. However, all these require a cranial US/CT scan to confirm the diagnosis and assess the prognosis. With frequent use of antenatal US, many cases are diagnosed in utero, thus planning the management in fetal/early neonatal period[2].

Once diagnosed, almost all hydrocephalic patients require treatment. Drugs like acetazolamide, Frusemide, Glycerol may be used temporarily, but their role as definitive treatment is not recommended[1]. Some patients had been found to have spontaneous arrest of hydrocephalus on long term follow up. Most of these cases are border line hydrocephalus and need regular monitoring to rule out progressive brain damage[3].

Current surgical treatment of hydrocephalus is VP shunt or VA shunt. The former is most commonly performed because of its technical simplicity and other advantages[1]. The past methods of diverting CSF into fallopian tubes, ureter or stomach are now obsolete. However VC shunt and ventriculo-pleural shunts are occasionally used as alternate procedures after multiple failures of VP shunt[4,5].

Complications following cerebro-spinal fluid shunts (CS shunts) are common requiring multiple revisions/ alternate procedures. A complication rate of 29 to 65% has been reported in literature[6].

Infection is the more serious complication after a CSF shunt and in some cases may prove fatal. Infections following VP shunt are less frequent and mild in severity as compared to VA shunt. Four to 9.4% of shunts may get infected in first 3 to 4 months after their insertion[7,8,9] and in most of these Staph aureus is the infecting organism[1,10,11]. However, H. influenzae may also be responsible in some cases occurring after 4 months of shunt placement[13]. Preoperative antibiotics have been shown to reduce the rate of shunt infection in many studies[1,12,14], but factors like multiple revisions, protein content of CSF, etiology of hydrocephalus except multi-located hydrocephalus[15] did not seem to have any effect on rate of infection.

Shunt blockage/malfunction is another common complication. Long-term follow up of shunted hydrocephalus patients has shown a shunt blockage/ malfunction rate of 81%[16]. The causes of blocked shunts are multifactorial but subclinical infection by Staph. aureus may be responsible in many. Both ventricular and peritoneal ends of the shunt may be blocked by blood/ choroid plexus, omental plug or protein exudate[1]. However blockage of catheter due to its fracture in neck[17], peritoneal CSF psueudocyst[18] may also be found in some cases. It has been seen that age of patient, type of surgery (Primary/Re-insertion) doesn't influence the rate of blockage, while cases of multiloculated hydrocephalus and those following meningitis or intraventricular hemorrhage are more prone to blockage[7,15]. The treatment of the blocked shunt is revision, but those with recurrent blockage may require alternate procedures in the form of VC shunt or ventricle-pleural shunt[4,5]. Rarely complications like visceral perforations-peritonitis, intestinal obstruction, shunt over drainage and epileptic seizures may also occur[18,19].

Going by the above discussion and analysis of our 50 patients, a complication rate of 30% is not excessive as against 29 to 65% reported in the literature. Three of our patients had infective complications (6%) as compared to 4 to 9.4% in different series. Shunt blockage has been our main problem in 9 patients (18%), however, three of these had spontaneous arrest of hydrocephalus and did not require any treatment. Thus only 6 patients (12%) required revisions of shunt. Various series have mentioned end of the shunt catheter. One patient each underwent VC and VA shunt because of repeated blockage of the VP shunt. Two patients who had intestinal obstruction were found to have functioning shunts at the time of laparotomy.

In summary we can say that 1) a cranial US is the most useful investigation for diagnosis of hydrocephalus in children, 2) VP shunt should be the primary surgical treatment of hydrocephalus, 3) spontaneous arrest of hydrocephalus may occur after surgery, but these children require a close follow up to detect any complication/ brain damage, 4) shunt complications like infection and blockage are inter related and frequent problems requiring early detection and alternate procedures in some patients, 5) preoperative antibiotics are effective in reducing the rate of shunt infection/blockage and should be routinely recommended.

Acknowledgement

The authors are highly thankful to M/s Eli Lilly Ranbaxy India Limited (Medical division) New Delhi for the help rendered in providing the references for preparing the manuscript.

References:

1. Epstein MH, Uclvarhelyu GB (1985). Spina bifida and hydrocephalus. In Pediatric Surgery, 4th. Edition. Welch KJ, Randolph JG, Ravitch MM et al. (Eds.) pp. 1425-1442.
2. Harrison MR, Filly R, Globus MS et al. Fetal treatment. N. Eng. J. Med. 1985; 307:1651.
3. Laurence KM, Coates S. The natural history ofhydrocephalus. Detailed analysis of 182 unoperated cases. Arch. Dis. Child. 1962; 37:345.
4. Kettof JA, Klein RL, Maukkassa KF. Ventriculo-cholecystic shunts in children. J. Pediatr. Surg. 1997; 32(2): 181-183.
5. Sanders DY, Summers R, DeRouen L. Symptomatic fluid collection of CSF caused by a ventriculo-pleural shunt. South MEd. J. 1997; 90(3): 345-346.
6. Di Rocco C, Marchese E, Velardi F. A survey of the first time complication of newly implanted CSF shunt devices for the treatment of non-tumoral hydrocephalus. Child Nerv. Syst. 1994; 10(5): 321-327.
7. Borgbjerg BM, Gjerris F, Albeck MJ et al. Frequency and causes of shunt revisions in different cerebrospinal fluid shunt types. Acta. Neurochirug. 1995; 136(3-4): 189-194.
8. Johnson DL, Conry J, O'Donnell R. Epileptic seizures as a sign of cerbrospinal fluid shunt malfunction. Pediatr. Neurosurg. 1996; 24(5): 223-227.
9. Brydon HL, Hayward R, Harkness W, Bayston R. Does the cerebrospinal fluid concentration increase the risk of shunt complications? B.J. Neurosurg 1996; 10(3): 267-273.
10. Lee JY, Wang KC, Cho BK. Functioning periods and complications of 246 cerebrospinal fluid shunts procedures in 208 children. J. Korean Med. Sci. 1995; 10(4): 275-280.
11. Ersashin Y, Mutluer S, Guralbag E. Cerebrospinal fluid shunt infections. J. Neurosurg Sci. 1994; 38(3); 161-165.
12. Lorenzetti C, Ramadan A, Favier J et al. Prevention of infections of cerebrospinal fluid shunts for hydrocephalus. Neuro. Chirurgie. 1994; 40(4): 233-241.
13. Ronann A, Hogg GG, Klerg GL. Cerebrospinal fluid shunt infections in children. Pediatr. Inf. Dis. J. 1995; 14(9); 782-786.
14. Haines SJ, Walters BC. Antibiotics prophylaxis for cerebrospinal fluid shunts: A metanalysis. Neurosurg 1994; 34(1): 87-92.
15. Jamjoom AB, Mohammad AA, Al-Boukai et al. Multiloculated hydrocephalus related to cerebrospinal fluid shunt infections. Acta Neurochirurg. 1996; 138(6): 714-719.
16. Whitehouse HE, Czosnyka M, Picard JD. Shunt audit: A computerized method for testing the performace characteristics of shunts in vitro. Child Nerv Syst. 1994; 10(3): 158-161.
17. Cuka GM, Hellbusch LC. Fractures of the peritoneal catheter of cerebrospinal fluid shunts. Pediatr. Neurosurg 1995; 22(2): 101-103.
18. Rainov N, Schobess A, Heidecke V et al. Abdominal CSF pseudocysts in patients with VP shunts. Acta. Neurochirugica. 1994; 127)1-2): 73-78.

Role of Elective Irradiation to Drainage Sites in Squamous Cell Carcinoma of the Skin Trunk and Extremities

Nazir A. Khan, M.D.; Shameem Akhtar, M.D.; Mohammed Y. Kharadi, M.D.; Wajahat H. Andrabi, Ph.D.
Mohammed A. Darzi, M.S.

Abstract: *Sixty patients with histopathologically proved squamous cell carcinoma of the skin were enrolled in the study. 30 patients (Group A) were studied prospecitvely and 30 patients (Group B) were taken as retrospective group for control. All patients had clinically node negative status at presentation. Primary site was treated by surgery alone or by combined modality (surgery followed by radiotherapy) in both the groups. In Group A the most susceptible echelon of lymphnode region was treated by elective irradiation. A dose of 45 Gy in 4 weeks with a daily fraction of 2.25 Gy and five fractions per week was delivered by a direct single portal using 60 Co unit. In Group B no elective irradiation was given. Patients were followed upto a period of 18 months. From the retrospective group (Group B), it was observed that 25 out of 30 patients (83.33%) developed regional nodal metastases within 6-12 months period after the treatment of primary lesion, and as a contrast in prospective group (Group A) one patient (3.84%) developed regional lymphnode metastases. However, local recurrence was observed in 3 and 6 patients in Group-A and B respectively. Elective irradiation was tolerated well by all patients. Elective irradiation has proven to be quite beneficial in controlling regional recurrences while treating squamous cell carcinoma of the skin of extremities and trunk regions.*

Key words: *Skin cancer, Elective irradiation, Lymphnodes.*

JK-Practitioner 1999; 6(1): 35-38

Introduction

Varied incidence of skin cancer has been reported from different centres all over world with an estimated annual incidence of more than 700,000 cases in U.S.A.[1] According to the report of W.H.O. the incidence from different centres in India varies from 1.9 to 9 percent. About 63.8 percent of these tumors are squamous cell carcinomas[6,7]. There are number of options available for the primary management of squamous cell carcinoma of the skin. The most commonly used treatment modalities are primary resection, radiation therapy and Moh's micrographic surgery[1]. Superficial nature of skin cancer makes it readily accessible to examination, thus represents the perfect model for cancer prevention, early detection and treatment[1]. Successful treatment will depend on ability to either modality to remove or ablate the malignancy, when it is still subclinical within regional nodes. There has not been yet any randomized study conducted regarding the treatment policy to be employed in the patients of squamous cell carcinoma of the skin with clinically negative drainage areas. However, there is a strong evidence of lymphnode metastases after the treatment of primary lesion within the first two years of follow up[2,8,5,3,]. The role of elective regional nodal irradiation in squamous cell carcinoma of the skin is really not known. However, the availability of high tech radiation with its various advantages has become an effective treatment modality for regional nodal prophylaxsis. It has the advantage of being able to treat a wide area of subclinical disease with little or no alteration of normal tissues thus allows it to produce excellent cosmetic results as well as a high chance of treatment success[4]. This study represents the first state wide attempt in treating patient with the elective nodal irradiation in squamous cell carcinoma of the skin. We have tried to find out the impact of the treatment on regional tumor control.

Methods and Materials

A total of 60 patients were enrolled in the study. Of these 30 patients were prospectively included in the study (Group A) and 30 patients were taken retrospectively in the control (Group B). This Group B patients were selected from those who were registered and treated at this centre from 1992 to 1995. Their clinical, pathological, treatment details and a follow up of 18

From the Department of Radiation Oncology (Khan, Akhtar, Prof. Kharadi) **Medical Physics** (Andrabi) **and Reconstructive Surgery** (Darzi) **SKIMS, Srinagar, Kashmir (India)**
Received May 1998 Accepted December 1998
Correspondence to : Prof. M.Y.Kharadi, Deptt. of Radiation Oncology, SKIMS, Soura, Srinagar-190011, Kashmir (India) GPO Post Bag No. 27, Phone 0194-477064 Ext. 425,274, Fax : 0194-473470, E-mail = root@skims.ren.nic.in

months was available from the treatment of primary lesion. All patients had to fulfill following criteria for inclusion in this study:

1. Patients should have histologically documented squamous cell carcinoma of the skin, without clinical evidence of lymphnode involvement at presentation.
2. Primary lesion should have measured 2 or more than 2cm in longest dimension.

In all patients primary site was treated with surgery in the form of wide excision with approximation and or followed by Radiothrapy. In Group A the most probably echelon of lymphnode area was treated with elective irradiation. An incident (dose prescribed at Dmax) dose of 45 Gy over 4 weeks, with a daily fraction of 2.25 Gy and five fractions per week was delivered by a direct field on theraton 780 (60 Co-unit). The length of follow up was measured from the first day of radiation therapy to lymphnode region. Patients were followed upto a period of 18 months. The results of Group A were compared with Group B where no elective irradiation to drainage sites was given. For statistical analysis chi-square test was applied.

Results

A total of 60 patients were taken up for study. Of these there were 56 evaluable patients. Four patients from group 'A' were excluded from study because two patients left treatment in between and the other two patients developed lymphnode metastases at the start of Radiotherapy. Table-I gives the distribution of patients in the two groups as per the age, sex, and predisposing factors, Table-2 gives the distribution of patients as per the site, size and differentiation. There was no statistically significant difference between the two groups with respect to these factors, chi-square test was applied for analyzing the statistical difference. Majority of the patients in this study were within the age range of 41-60 years (45 out of 56 patients). Males were predominant with a male to female ratio of 1.8:1. In group 'A' commonest predisposing factor was erythema-ab-igne.

Commonest site of involvement was medial aspect of thigh (80.76%) and (50%) in group A and Group B respectively. Majority of the patients had lesion between 4-6cm in longest dimension of 46.16% and 46.66% in Group A and B respectively. Patients had well differentiated type of histology in 84.62% and 83.33% in group A and B respectively. The treatment of primary lesion was chiefly surgical and in seven cases post-operative radiotherapy was given. In these cases surgery performed was inadequate, as resection lines were involved with the disease. A dose of 50 Gy. in 25 fractions with a fraction size of 2 Gy was delivered. Primary lesion in none of the patients was treated by radiotherapy alone.

Table-1: Pretreatment Characteristics

Characteristics	Group A (n=26) No. of Pts.	%age	Group B (n=30) No. of Pts.	%age	Statistical inference
Age in years					
<40	03	11.53	05	16.66	
41-60	22	84.63	23	76.67	p>0.5
>60	01	03.34	02	06.67	N.S.
Sex					
Male	15	57.69	21	70	p>0.10
Female	11	43.13	09	30	N.S.
Predisposing Factors					
Erythema-ab-igne	13	50	09	30.01	
Trauma	0	0	02	06.66	p>0.1
Burns	0	0	02	06.66	N.S.
Unknown	13	50	17	56.67	

n= Total No. of patients, Pts. - Patients

Elective irradiation was administered to the most susceptible echelon of lymphnode region of the primary site in Group-A. A dose of 45 Gy in 4 weeks was delivered by direct anterior portal on theraton-780 (60 Co Unit). Duration between the surgery and start of radiotherapy was kept minimum of one month. Follow-up was started from the first day of Radiotherapy and continued upto a period of 18 months.

Table-2: Pretreatment Characteristics

Characteristics	Group A (n=26) No. of Pts.	%age	Group B (n=30) No. of Pts.	%age	Statistical inference
Site					
Thigh	21	80.76	15	50.00	
Ant. Abdominal Wall	02	07.72	04	13.34	
Ant. Chest Wall	01	03.84	00	00	
Arm	01	03.84	00	00	
Hand	00	00	01	03.33	p<0.5
Leg	00	00	05	16.66	N.S.
Foot	01	03.84	04	13.34	
Sacral Region	00	00	01	03.33	
Longest Dimension Size in cm					
2-4	10	38.46	09	30.00	
4-6	12	46.16	14	46.66	p>0.5
>6	04	25.38	07	23.33	N.S.
Differentiation					
Well	22	84.62	25	83.33	
Moderately	02	07.69	02	06.67	p>0.5
Poor	02	07.69	03	10.00	N.S.

Toxicities with the elective irradiation were managed conservaitvely, with no patient requiring dose modification or postponement of planned radiotherapy protocol. Five patients developed mild skin reactions [3 patients mild erythma (GI), 2 patients dry desquamation (G2)]. One patient developed reactive lymphedema of the involved leg. While as 20 patients out of 26 developed no reactions.

Nodes were considered to be involved when they showed histologic evidence of metastases. One patient (3.84%) in group A and 25 patients (83.33%) in group B developed regional lymphnode metastases within 6-12 months period of follow up. Three patients in group A and six patients in group B developed local recurrence. In these cases primary lesion was treated by surgery alone. None of the patients in this study developed distant metastases.

Discussion

The key to effective treatment of skin cancer lies in early detection and adequate initial treatment. Virtually all skin cancers begin as small easily controlled lesions, that can be successfully treated in a variety of ways with a minimum of morbidity and a favourable outcome. By contrast extensive and recurrent skin cancer presents a difficult challenge for cure, with complex surgical or radiation therapy[1]. There is high incidence of lymphnode metastases in lesions involving arms, legs, feet, and increases when a recognizable precancerous condition has been present for a considerable time[8]. Same were the reasons responsible for high incidence of lymphnode metastases in our study. Majority of the patients in both the groups had lesions between 4-6cm in greater dimension at presentation (Table-2). Which is in accordance with the data in literature[6,8]. Majority of patients had chronic precancerous conditions (erythema-ab-igne) in 50% and 30% of cases in group A and B respectively. Surprisingly maximum number of patients in this study had well differentiated type of histology 84.62% and 83.33% in group A and B respecitvely. It seems that squamous cell carcinoma of the skin is less aggressive. However, the degree of differentaiation of a tumor does not necessarily determine its aggressiveness and limit the spread of disease. Out of 30 patients in group B 25 (83.33%) developed regional nodal metastases within a period of 6-12 months after the treatment of primary lesion. This is in accordance with the data reported by Glass RL[3] and Taylor, Nathanson and Shaw[8] who found lymphnode metastases 75 percent and 65 percent in axillary and inguinal regions at follow up of less than 3 years. By contrast one patient 3.84% developed regional nodal metastases at two months follow up in group A. It justifies the role of elective nodal irradiation being statistically significant ($p<.001$) chi-square test with yates correction was applied for analyzing this statistical significance. Elective irradiation to drainage sites was associated with minimal toxicities. This was tolerated well by patients. A dose of 45 Gy in 4 weeks with a fraction size of 2.25 Gy was found to be adequate to control the subclinical disease in lymphnodes. Very little is known regarding the treatment policy to be employed in the patients of squamous cell carcinoma of the skin of extremities and trunk with clinically negative drainage areas. The ability to identify nodal disease prior to its manifestation that is while the deposits are small or remain in subclinical state is limited. It is probable that if regional lymphnode dissection is carried out as soon as node enlargement becomes evident, the results will be nearly as good as to when elective dissections are employed. The policy of watchful waiting involves frequent and conscientious follow up observation and depends upon the complete and intelligent co-operation of the patient[8]. Differences of opinion will exist as to whether elective dissection is justifiable in the absence of palpable lymphnodes, the high incidence of metastases in the carcinoma of arm, leg and foot justifies the performance of elective dissection. Furthermore, the high incidence of metastases in cases originating from chronic precancerous lesions strongly argues for elective dissections[8]. It is clear from the literature that elective lymphnode dissection has been tried but results are disappointing because it is associated with high morbidity and high recurrence rates 27-60%[2,3,8]. There is a strong evidence of lymphnode metastases in skin cancer, despite of this nodal irradiation has not gained acceptance due to the controversies regarding the irradiation of non-disease region[5]. The role of elective irradiation to lymphnode regions is really not known in squamous cell carcinoma of the skin. However, the availability of high tech-radiation equipments with its various advantages has become an effective alternative management modality for regional nodal prophylaxis. Radiation therapy has definite advantages over surgery.

Conclusion

On the basis of the encouraging results, we recommend elective irradiation to the clinically negative regional lymphnodes in addition to prompt and though surgical treatment of the primary lesion in treating the squamous cell carcinoma of the skin of trunk and extremities. This most common of all curable cancers lends itself to cancer control methods and should never be allowed to progress to a stage when it becomes a major therapeutic problem or a major cause of patient morbidity.

References:

1. Fleming, I.D.; Amonette, R.; Monaghan, T.: Fleming, M.D. Principles of management of basal and squamous cell carcinoma of the skin. Cancer 1995; 75 (suppl): 699-703.
2. George, T.K.; Sontagnese, A.D.; Benett, I.M. Chemotheraphy for metastatic merkel cell carcinoma. Cancer 1985; 56: 1034-1038.

3. Glass, R.L., Spratt, J.S.; Perez-Mesa, C. Epidermoid carcinoma of lower extemeties: An analysis of 35 cases. Arch. Surg. 1964; 89: 955-960.
4. Lovett, R.D.; Perez, C.A.; Shapire, S.J.; Garcia, D.M. Extemal irradiation of epithelial skin cancer. Int. J. Radiat. Oncol. Biol. Phys. 1990; 19: 235-242.
5. Raaf, J.H.; Urmacher, C.: Knapper, W.K.; Shiu, M.H.; Cheng, W.K. Trabecular (Merkel cell) carcinoma of the skin. Treatment of primary, recurrent and metastatic disease. Cancer. 1986; 57: 178-182.
6. Sanyal, B.; Shastri, S.R.; Hakim, A.; Kharadi, M.Y.; Tikku, J.L.; Verma, A.; Rasool, SS; Pathania, A.G.S. A clinical profile of skin cancer from Kashmir valley with special reference to "Kangri" cancer. J. Clin. Radiot. and Oncol 1989; 4: 31-06.
7. Talvalkar, G.V. Squamous cell carcinoma of the skin. Its incidence and etiopathogenesis in 625 cases. Ind. J. Cancer 1970; 24-33.
8. Taylor, G.W.; Nathanson, I.T.; Shaw, D.T. Epidermoid carcinoma of extremeties with reference to lymphnode involvement. Ann. Surg. 1942; 113: 268-275.

With Best Compiments from

JAY AAR AGENCIES

IST FLOOR, K.C. PLAZA, RESIDENCY ROAD, JAMMU TAWI

Distributors for :

★ HOECHST MARION ROUSSEL LTD.
★ KNOLL PHARMACEUTICALS LTD.
★ LUPIN LABORATORIES LTD.
★ MACMILLON PHARMACEUTICALS LTD.
★ NICHOLAS PIRAMAL (INDIA) LTD.
★ SMITH KLINE BEECHAM PHARMACEUTICALS LTD.
★ WIN MEDICARE LTD.

JAY AAR AGENCIES
PHARMACEUTICAL DISTRIBUTORS

Clinical Profile and Management of Ectopic Pregnancy in Kashmir

Bilquees Jamila M.D.; Nighat Firdous, M.D.; Israh Akhtar M.B.B.S.

***Abstract:** Patients with ectopic pregnancy managed surgically at the Lal-Ded Hospital, Srinagar, the Medical College associated hospital for Obstetrics and Gynecology, over a perid of 8 years is described. Total number of cases treated surgically during this period was 280 out 326 referred for the evaluation of suspected Ectopic pregnancy. Diagnosis was established on the basis of clinical features supplemented by abdominal ultrasonography and/or diagnostic laparoscopy. All the cases were subjected to surgery. Predisposing causes included Intra-uterine contraceptive device usage, Pelvic inflammatory disease, previous tubal surgery. The commonest clinical presentation was abdominal pain, vaginal bleeding, syncopy and shock. Salpingectomy or salpingo-oophorectomy was the usual technique depending upon the ease of surgery and operative findings. There was no operative or post-operative mortality.*

***Key words:** Ectopic Pregnancy, amenorrhea.*

JK-Practitioner 1999; 6(1): 39-40

Introduction

There has been tremendous progress in the management of Ectopic Pregnancy (EP) over the last decade particularly the non-surgical expectant management of EP by use of methotrexate[1]. Diagnostic accuracy has been considerably increased by endovaginal sonography[2] and serial β HCG analysis. However a good number of patients present with the more profound symptomatology like hypotension or shock therefore requiring urgent surgical intervention. Due to non-availability of routine endovaginal sonography and HCG estimation in our hospital, diagnosis mainly rests on clinical assessment, abdominal ultrasound and/or diagnostic laparoscopy. A high index of suspicion in a given patient has been the cornerstone of management of such patients although pelvic inflammatory disease (PID) is considered a predisposing cause[3], the occurrence of EP has been mostly associated with the use of intrautrine contraceptive device (IUCD) in our patients more commonly, possibly being the contraceptive method of choice in our State. Surgical treatment by salpingectomy with or without oophorectomy has been uniformly successful with zero mortality.

Material and Methods

The study was conducted from August 1989 to August 1997 in 326 consecutive patients suspected to have EP on the basis of clinical features of amenorrhea, abdominal pain, vaginal bleeding, syncope, adnexal or abdominal tenderness or mass. Forty six patients in whom abdominal ultrasound and/or diagnostic laparoscopy showed no features of ectopic pregnancy were excluded. The remaining 280 cases in whom EP was confirmed were subjected to either salpingectomy or salpingo-oophorectomy.

Results

A total of 280 cases were confirmed to have EP. The overall percentage EP over a period of 8 years was 0.24 (table 1). Majority of our patients were aged less than 30 years and most of the ectopic pregnancies occurred in women with one or two previous pregnancies although a signficant number of EP did occur in relatively younger patients with multiparity. Out of a total of 112 EP in the patients in the age group 20-25 years, 49 were 1 or 2 para and 45 were 3 or 4 para. This trend however was not seen in other age groups (table 2).

Table-1: Incidence of ectopic pregnancy from 1989 to 1997

Year	Total No. of deliveries	No. of ectopic pregnancies
1989-90	13502	30
1990-91	11076	31
1991-92	13870	35
1992-93	14616	36
1993-94	14833	37
1994-95	16454	36
1995-96	15751	37
1996-97	16007	38
Total	116109	280

From Department of Obstetrics and Gynaecology Govt Medical College Srinagar, Kashmir (India) (Prof. Bilquees, Nighat Israh)

Received Oct. 1998 **Accepted Dec. 1998**

Correspondence to : Prof. Bilquees Jamila, Head Deptt. of Obst & Gynac. GMC, Srinagar.

Table-2: Relation of age and parity in 280 cases of ectopic pregnancy

Age in years	Parity 0	1-2	3-4	5 or more	total
Less than 20	15	-	-	-	15
21-25	8	49	45	10	112
26-30	6	47	30	10	93
31-35	4	30	10	3	47

The predisposing factors in the majority the patients were history of intrauterine contraceptive device (IUCD) insertion, Pelvic inflammatory disease (PID), prior EP with salpingectomy or previous caesarian section with tubal ligation or appendectomy. On hundred and fifty one cases belonged to the group of either IUCD insertion or PIUD (Table-3).

Majority of the patients presented with abdominal pain, vaginal bleeding, and/or hypotention or shock. Only 10 cases did not complain of abdominal pain. Tender abdomen or cervix and adnexal tenderness were the commonest findings on examination.

The management strategy comprised of surgical intervention by either salpingectomy or salpingo-oophorectomy. In only 10 cases milking of the tube was possible obviating the need for such surgery.

Table-3: Predisposing factors in 280 cases with EP

Risk factors	Number	%age
History of infertility	26	9.28
History of IUCD insersion	91	32.5
History of PID	60	21.4
Prior EP and salpingectomy	23	8.2
Prior tubal surgery	10	3.5
Appendicectomy	21	7.5
Prior lscs with tubal ligation	23	8.2
Gonadotrophin therapy	5	1.7

Discussion

It is evident from these results that the commonest predisposing factor for EP in our patients was prior IUCD insertion. It is pertinent to known that this form of contraception is very popular in this part of the country and is perhaps the commonest method of spacing. It is a known fact that IUCD insertion increases the risk of EP[4,5]. Chow et al[4] have observed that current use of an IUCD besides other factors like PID or pelvic surgery has a strong association which increaes incidence of EP. Makinin[6] has reported that the incidence of EP is the highest in Finland because approximately 25-30% of the female population aged 15-44 use IUCD as the method of contraception. PID is a common predisposing cause of infertility as well as EP[7]. Of 280 case 60 belonged to this group. PID is a common predisposing factor in the western countries. It ranked 2nd in our cases and accounted for 22% of all EPs. Chow et al have observed that PID is responsible for increase in EP in all age groups. In our patients PID is likely as a result of non-gonococcal pelvic infections as the incidence of STD is quite low here and the chlamydial infections may be playing more important role. PID is also responsible for infertility and 26 of our patients had history of infertility and 17 of them had PID.

Abdominal pain, bleeding PV and amenorrhea were common in our patients. Most of the patients referred to our hospital were either in severe hypotention or shock due to intraperitoneal bleeding following ruptured EP needing immediate resuscitation and intervention. This usually was because low literacy level in our patients and lack of proper healthcare delivery system in the peripheries. In the patients who came early, diagnostic laparoscopy was performed to confirm EP.

In our series, salpingectomy or salpingo-oophorectomy was the procedure of choice because majority of them presented in severe hypotention or shock. After intial rescucitation and blood transfusion, laparotomy was performed under general anesthesia. No operative or post-operative mortality was observed. In 10 patients milking of the tube was possible. Follow up was uneventful in all the cases. Future reproductive function is very important. In women who have yet to complete their family or have no child. Conservative surgery like linear salpingostomy and manual expression of the products of conception from the ampulla of the tube and above all very early detection by serial HCG and endovaginal ultrasound would be quite appropriate and useful to manage such cases. However such treatments nor only requires operative experative but the latter diagnostic modalities are not routinely available.

References:

1. Korhonen J, Stenman UH, Yi Ostalo P. Low dose methotrexate with expectant management of ectopic pregnancy. Obstetr gynecol 1996; 8(5): 775-78.
2. Atrim et al. role of endovagnial sonography in the diagnosis and management of ectopic pregnancy. Radiodiagnosis 1996; 16: 755-74.
3. Kasule J and Seeras R. Ectopic tubal pregnancy in Zimbabwe. J obstet gynecol 1989; 9: 180-83.
4. Chow W-H, Daling JR, Cates W Jr, Greenberg RS. Epidemiology of ectopic pregnancy. Episemio rev 1987; 9: 70-94.
5. Hallatt Jg. Ectopic pregnancy associated with the intrauterine device: a study of seventy cases. Am J of Obstetgynecol 1976; 125: 754-58.
6. Makinen JI. Ectopic Pregnancy in Finland 1967-1983: A massive increase. Brt. Med. J 1987; 294: 740-41.
7. Blythe MD. Pelvic inflammatory disease in the adolescent population. Semin pediatr surg 1998; 7:43-51.

Epidemiology of Perinatal Mortality A Hospital Based Study

Farooq Fazili; G.M. Mattoo.

***Abstract:** Perinatal mortality, being considered as a sensitive indicator of the health status of community; a study was undertaken to see the effect of various epidemiological correlates on the perinatal mortality observed in the population attending our Maternal and Child Health Hospital at Sher-i-Kashmir Institute of Medical Sciences, Srinagar for a period of one year from Jan. 1994 to Jan. 1995. In this study the total perinatal mortality rate (PNMR) observed was 43.1 per 1000 total births, where as the still birth rates (SBR) and early neonatal death rates (ENDR) observed were 27.5 and 16.0 per 1000 births respectively. The PNMR was found to be almost six times more in multiple births as compared to singleton births. PNMR was significantly higher in illiterate mothers, in extremes of age, those living in joint families and having incomplete antenatal care. PNMR was found low in higher socioeconomic class. Maternal weight was found to have significant effect on perinatal loss, whereas maternal height was having insignificant effect on perinatal outcome.*

***Key words:** Perinatal mortality rate, Still birth rate, Early neonatal death rate.*

JK-Practitioner 1999; 6(1): 41-45

Introduction

Perinatal mortality reflects the amount of pregnancy wastage due to fetal and neonatal deaths and is being taken as a sensitive indicator of maternal and child health status in particular and health status of community in general.

Perinatal mortality (PNM) is a problem of serious dimensions in all countries. It now accounts for about 90 percent of all fetal and infant mortality in developed countries being 15 per 1000 births in England and Wales (1979)[1], 22 in USA (1975)[2], 10.4 in Singapore and 8.0 in Japan (1975)[2]. The lowest rate is in Sweden i.e. 6.0 per 1000 births (1984)[3]. On the other hand in developing countries which constitute about 72 percent of the world population, the magnitude of perinatal mortality is quite high necessitating to focus the full attention towards this problem[4]. The perinatal mortality rate (PNMR) being of the magnitude of 71 per 1000 births in Dhaka Bangladesh (1983)[2]; 50-55 in Korea (1976)[5], 34.6 in Malaysia (1976)[5] and 32.07 in Philippines (1976)[5].

PNMR in India, 'a developing country' is 5-6 times higher as compared to developed countries[6]. About 1.5 million perinatal deaths occur every year in India.[7] The estimation of perinatal mortality rate in India according to the sample registration system is reported to be 53.1 in rural aveas; 34.5 in urban areas and 49.6 combined in rural and urban areas in 1988[8]. Although there has been a marked reduction in India's PNMR over last few decades reducing it from 182 per 1000 births in 1930[5] to 49.6 per 1000 births in 1988[8]. Visualizing the incidence of PNMR in India it is quite essential to pay considerable attention to the control of its magnitude in the positive direction, especially when the national goal set for the year 2000 AD in 30-35 per 1000 birth.[8]

Consequently it seems imperative to see the magnitude of PNM in this part of the country and further to study the role of various epidemiological factors in general having their influence on the perinatal outcome.

Material and Methods

The study was conducted in the Obstetric unit of Maternal and Child Health Hospital and Deptt. of Neonatology of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir for a period of one year from Jan. 1994 to Jan. 1995. Perinatal mortality in this study, has been taken in accordance with the definition given by WHO study group on perinatal mortality[4] i.e. fetal and neonatal mortality occuring from 28th week of pregnancy until the end of first week of life, thus including stillbirths and early neonatal deaths.

All perinatal deaths which occurred in this hospital during the period of study were recorded in detail on the comprehensive pretested schedule. Any baby who was referred to neonatal intensive care unit after birth was followed there till the end of first week of life.

In order to estimate the strength of association of perinatal mortality with various epidemiological correlates, another sample of 200 mothers giving birth

---

From the Department of Community Medicine, SK Institute of Medical Sciences, Srinagar (Fazili, Mattoo)

Received May 1998 **Accepted November 1998**

Correspondence to : Dr. Farooq Fazili, Sr. Resident M.C.H., Department of Community Medicine, SK Institute of Medical Sciences Srinagar-190011, Post Bag No. 27, Kashmir India.

to normal neonates selected randomly was also studied in an identical manner which served as a control.

The data thus obtained was analysed and inferences drawn are tabulated and subjected to various statistical tests to get the significance of various factors affecting the perinatal mortality.

Observations and Results

There were total 2162 deliveries in the hosptial during the study period with 2145 singleton and 17 multiple births. Multiple births included 16 twins and one triplet thus making a total of 2180 births. The overall perinatal mortality rate (PNMR) is 43.1 per 1000 births with still birth rate of 27.5 per 1000 total births and early neonatal deaths rate of 16.0 per 1000 live births. The perinatal mortality rate (PNMR) in multiple deliveries observed was 228.5 per 1000 births as compared to the PNMR of 40.1 per 1000 births in singleton births.

Table 1 shows the influence of various epidemiological factors on perinatal outcome. As is evident from the table, the residence is not showing any significant effect on perinatal loss. Majority of cases in both the groups were from urban areas. Higher percentage (84.44%) of maternal cases having perinatal loss belong to joint families as compared to nuclear families (15.56%) and the effect of type of family has been found highly significant on perinatal loss. Maternal literacy is showing significant effect on perinatal loss. The percentage of iliterate mothers was more in study group involving perinatal loss as compared to normal control group. The paternal illiteracy has also been found significantly associated with the poor perinatal outcome. The table further shows that the perinatal loss was more in mothers who were having incomplete antenatal care. The percentage of the maternal cases with incomplete antenatal care was more in study group with perinatal loss (52.2%) as compared to normal control group without perinatal loss (20.0%) and the difference was found significant statistically. The number of cases belonging to socioeconomic group I and II have been found to be higher in normal control group as compared to study group in which more number of cases belonged to socio-economic group III, thus showing a positive effect of socioeconomic status on perinatal loss although insignificant statistically.

There is a higher PNMR of 84.7 and 54.5 per 1000 births in mothers having less than 20 years and above 35 years of age respectively. In maternal age group of 20 to 35 years the PNMR ranges from 37.0 to 43.4 per 1000 births. The high mortality rate in two extreme age group of mothers have been found insignificant statistically.

Table 1: Influence of various epidemiological factors on perinatal outcome

Epidemiological Factors	Maternal Cases Study Group I involving perinatal deaths		Normal Control Group II with with no perinatal loss		X^2	P value & Significance
	No.	%	No.	%		
A Residence						
I Rural	28	(31.1)	52	(26.0)	0.810	>0.05 (insignificant)
II Urban	62	(68.9)	148	(74.0)		
B Type of family						
I Nuclear	14	(15.56)	62	(31.0)	9.674	<0.01 high Significant
II Joint	76	(84.44)	138	(69.0)		
C Maternal Literacy						
I Illiterate	33	(36.7)	44	(22.0)	9.87	<0.05 Significant
II Literate	57	(63.3)	156	(78.0)		
D Paternal literacy						
I Illerate	24	(26.7)	29	(14.5)	12.719	<0.05 Significant
II Literate	66	(73.3)	171	(85.5)		
E Antenatal Care						
I Complete	43	(47.8)	160	(80.0)	30.69	<0.001 Highly Significant
II Incomplete	47	(52.2)	40	(20.0)		
F) Socioeconomicd status						
I S.E. Group I	05	(5.5)	24	(12.)		
II S.E. Group II	52	(57.8)	124	(62.0)	4.15	>0.05 Insignificant
III S.E. Group III	33	(36.7)	52	(26.0)		

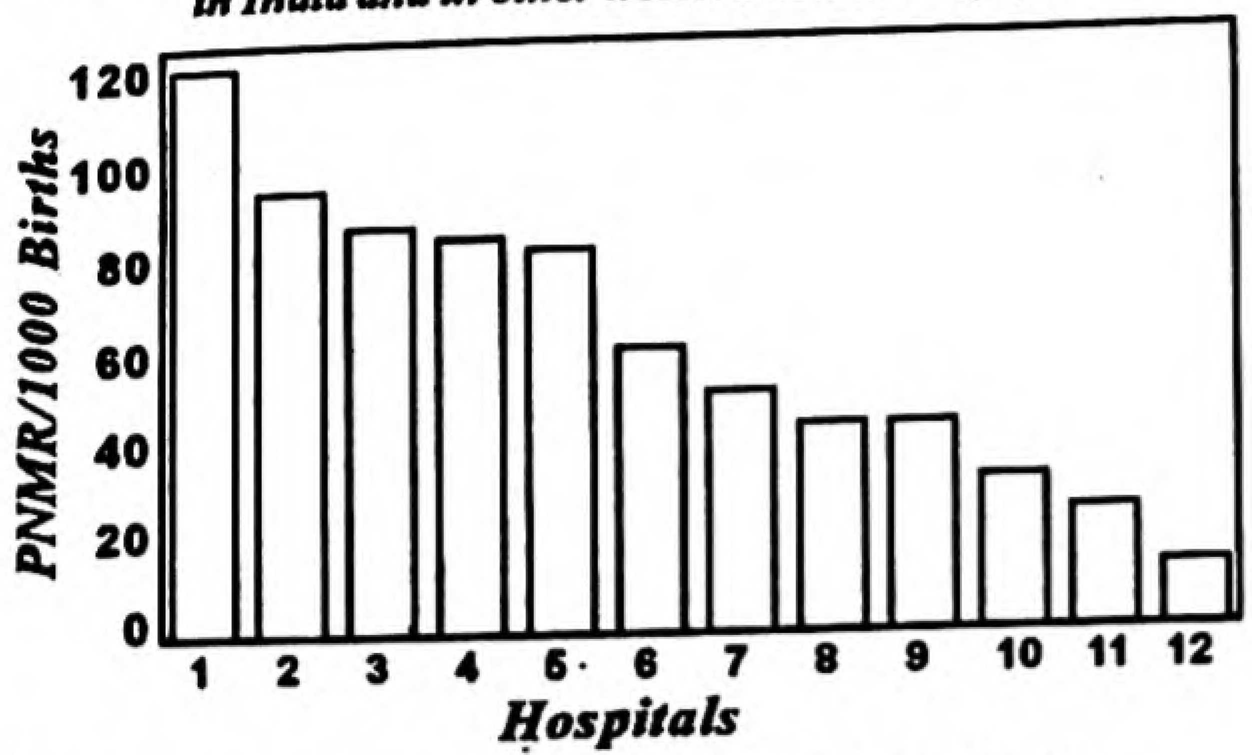
The mean weight of mothers in study group was 54.18±6.03 kg as compared to 55.975±4.72 kg in normal control group and the mean difference of 1.795 was found statistically significant at $p<0.05$. While the mean difference of 0.431 in height between the two groups has been found insignificant statistically.

Discussion

Perinatal mortality reflects the overall health care, especially the maternal and child health care services rendered in a community. Holland E[9] was one of the first to make a detailed study of still births and neonatal deaths, bringing out a comprehensive report based on careful histological examinations. Some of the notable contributions towards the study of perinatal mortality in our country have been made by Balfour R[10], Bajpai P.C.[11] and Mehdi Z[12].

In the present study we observed a perinatal mortality rate of 43.1 per 1000 total births which is comparatively lower than other hospital based studies in India but it is higher when compared with studies from western counttries (Fig. I). There were 94 perinatal deaths out of a total of 2180 births in our hospital during the study period in which there were 60 late fetal deaths and only 34 early neonatal deaths thus giving higher stillbirth rate (SBR) of 27.5 per 1000 total births as compared to ENDR (16.0/1000 births). This higher SBR as compared to lower ENDR has also been observed in other studies[11,13,14,15]. There being a well developed neonatology deptt. in this hospital with tertiary care facilities available, the ENDR is expected to be low.

Fig.1 Incidence of perinatal mortality in various hospitals in India and in other western countries (%)



1. Queen Mary's Hospital Lucknow (Bajpai PC 1966)[11]
2. Hospital for Madras (Santhance Krishan et al 1986)[30]
3. K.N.M. Hospital Allahabad (Agarval U.K et al 1982)[13]
4. Osmania General Hospital (Mehdi Z et al 1961)[12]
5. Simpson Memorial Hospital Edinburgh (1943-45)[12]
6. JIPMER Pondicherry (KamaSwam C et al 1993)[14]
7. Bellevae Hospital New York (1933-93)[12]
8. MCH Unit, SKIMS Soura, Srinagar 1995 present study
9. SAT Hospital Travindrum (Seguna Bai NS et al 1991)[15]
10. Southern Brazil (Barros FC 1987)[23]
11. Herman Hospital Houstan Taxas (1948-50)[12]
12. Chicago Lyingin Hospital (1946-49)[12]

In this study perinatal mortality has been found more than six times higher in multiple births (228.5 per 1000 births) as compared singleton births (40.1/1000 births). The high PNMR in multiple births has also been observed by others. Mehdi Z et al[12] have found PNMR of 267.5/1000 births in case of twin deliveries at O.G. Hospital and 267.6/1000 births at Govt. Maternity hospital Hyderabad. Kasturilal and Jamihal[16] have found high PNMR of 375/1000 births at Gulbarga in multiple births, where as Shah-Usha[17] has found still higher PNMR of 454.6/1000 births in twin deliveries at Maharashtra. The higher PNMR in multiple births have been attributed to prematurity, low birth weight, maternal complications and obstetric manoeuvers. This is a matter of great concern which can compound many times the effect of other factors influencing mortality common to all births.

Residence:

In the present study the rural or urban background of mothers was not found to have a significant association with the perinatal mortality. This finding is in agreement with that of Rao & Inbarj[18] at Tamilnadu who have observed insignificant difference with regard to the place of residence and perinatal mortality. The higher incidence of mothers from urban areas in the present study is because this hospital mainly serves the urban population.

Type of family:

The perinatal mortality in joint families was found to be far higher as compared to those living in nuclear type of families. Our results are in resonance with those of Mehdi et al[12] and Baird D[19]. High PNMR in large joint families may be attributed to the lack of proper care to pregnant women and children as they get diluted in this environment.

Literacy:

Perinatal mortality has been found closely related to the literacy status of parents. Mehdi Z et al[12], Singhel P.K. et al[20], Bhat I.A. et al[21] and Ramoeoa A[22] have observed high perinatal loss in illiterate mothers. This fact is also revealed by the present study, where we have found that more illiterate mothers were in study group with perinatal loss as compared to normal control group. The lesser perinatal loss in literate mothers may be attributed to the fact that literacy makes them more health conscious and thus helps in utilization of the health care services available to them in the community.

Antenatal care:

The present study shows that antenatal care strongly inflecence the perinatal outcome ($p<0.001$). Our results are in agreement with the observations made by other workers[11,13,14,16,20,23,24,25,26]. The antenatal care provides the tool for screening of high risk cases and keep them under constant surveillance thus improving perinatal outcome. All efforts should, therefore be directed to motivate mothers for antenatal check ups through health education of masses, paramedical health workers for maximum registration of pregnant women and continuous monitoring for timely intevention of high risk cases.

Socioeconomic status:

According to Peckhem C.S. et al[1], there is a strong association between perinatal mortality and social class of the father. The lowest rates occur in higher social class group and highest in children of unskilled manual workers. A close relationship between poor social conditions and high perinatal loss has been observed in various studies[11,16,20,23,27]. This relationship has also been observed in the present study but the results are insignificant statistically. The probable reason being that both the groups were represented mostly by middle class popultion and were more health conscious.

Smoking:

Smoking in pregnant women was a rare habit in the subjects of our study. Only six mothers among all registered cases were having the history of smoking during their pregnancy, with four cases in study group losing their babies in perinatal period and only two in the control group. Smoking has been found to be associated mainly with low birth weight than with poor perinatal outcome.

Maternal age:

The influence of maternal age on perinatal mortality has been found by various workers like Bajpai P.C. et al[11], Mehdi Z et al[12], Agarwal V.K. et al[13], and Barros F.C. et al[23]. Our findings are in general agreement with the observations made by these workers. The lowest perinatal loss in found in the group of 20-35 years (of mothers) and there is rise in the perinatal mortality when the maternal age is below 20 years or above 35 years. Bajpai P.C. et al[11] has attributed high PNMR in extreme age group to the increasing incidence of birth trauma and placental insufficiency with advancing age. Nayak A.H. et al[29] in their study at Bombay have reported higher PNMR in teenage group mothers and have attributed this to the increased obstetric complications like pregnancy induced hypertension (PIH), anemia, preterm labour, obstructed labour and birth trauma.

Maternal nutritional status:

Poor nutritional status of mother (e.g. anemia, short status and low maternal weight) influences the perinatal outcome adversely[21]. In the present study it has been observed that maternal weight has a significant effect on perinatal loss. Our observations are in agreement with Barros F.C et al[23] who in their study at Southern Brazil found that there is four fold increase in perinatal mortality in mothers who weighed less than 55kg. Maternal height did not appear to have any impact on perinatal outcome. Barros F.C et al[23] has also found insignificant association between maternal height and perinatal loss. Baird et al[10] and Shah Usha[17] have found higher perinatal loss in small mothers. It may be concluded that maternal height is not an important parameter for predicting the perinatal outcome but the maternal weight has significant impact on the perinatal outcome as the maternal weight is directly related to the nourishment and growth of foetus than her height.

Recommendations:

An overall socioeconomic development is necessary to improve the health status of the population and thus bringing down the morbidity and mortality during the perinatal period:

- By improving the literacy status of the community an increased participation in utilizing the health care services is expected which in turn will improve their health status and will bring down the perinatal loss.
- The best maternal age for child bearing has been found between 20 to 35 years and is carrying least obstetric and neonatal complications.
- For better perinatal outcome improved nutritional status of mother is required through proper antenatal care and further the early identification of high risk pregnancies and their proper timely interventions will also reduce the perinatal loss.

References:

1. Peckham CS et al. Pregnancy, child birth and perinatal mortality. (Chapt.33). Epidemiology of diseases. Ed. by D.L. Miller and RDT Farmer, published by Blackwell Scientific Publications LTd, Oxford, London, Edinburgh, Melbourne 1982, 412-51.
2. Perinatal mortality. Text book of Obstetrics and Neonatiology Ed. by D.C. Dawn. Dawn Books. Publ. by Sremoti Arati Dawn BA. 25 BCIT Road Sch. 52 Calcutta 14, 1990, 34-38.
3. Perinatal determinants of child survival. Workshop proceedings Feb. 20-23 (1989) ICMR, New Delhi Pub. at Central Electrical Press A12/1 -naraina India. Area Phase-1, New Delhi 110028.
4. Perinatal mortality and morbidity. WHO chronicle June 1971, 25(6): 267-74.
5. Singh KN, Mir NA. Perinatal mortality in South east Asia, (Chapt. 8) Current trends in perinatal medicine Srinagar Ed. by N.A. Mir & M. Hassan. Pub. by Vishinath Press Srinagar 1987, 39-48.
6. Augustine Teresa, Bhatia BD. Early neonatal morbidity and mortality pattern in hospitalized children. The Indian Jr. Pediatr 1986, 53(3), 323-25.
7. Singh Meherban. Special Article. Hospital based data on perinatal aned neonatal mortality in India. Indian Pediatr 1986: 23, 579-84.
8. Perinatal mortality, Park's textbook of preventive and social medicine. Pub. by Banarsi Das Bahanot 1167 Prem Nagar, Nagpur Road Jabulpur 482001 India 1994 p334-35.
9. Holland E. Report No. 7 Ministry of Health London 1922.
10. Balfour MP. Indian Med. Gaz. 1930, 65; 613.
11. Bajpai PC et al. Observations on perinatal mortality. Indian Pediar. 1996, 3(3), 83-98.
12. Mehdi Z et al. Incidence and causes of perinatal mortality in Hyderabad Andhra Pradesh India. Indian Jr. Med. Res. Sep. 1961: 49(5): 897-936.
13. Agarval VK et al. Some observations on perinatal mortality. Indian Pediatr. 1982, 19:233-38.
14 Kiameswaran C et al. Perinatal mortality. A hospital based study. Indian J. Pediatr 1993; 30(8): 997-1001.
15. Suguna Bai NS et al. Perinatal mortality rate in South Indian population. J. Indian Med. Assoc. 1991; 89(4); 97-98.
16. Kasturilal and Jammilal JH. Factors associated with perinatal mortality. Indian Pediatr 1974; 11(11): 743-47.
17. Shah Usha. Symposium on perinatal mortality. Perinatal mortality in India. Can it be reduced through primary health care? Indian J Pediatr 1986; 53: 327-31.
18. Roa PSS and Inbary SG. Extent of perinatal loss in South Indian Urban and rural population. Indian Pediatr. March 1975; 12(3): 221-27.
19. Baird Dugald. Perinatal mortality. The Lancet 1969; 8: 511-

15.
20. Singhal PK et al. Perinatal mortality in ICDS urban slum area. Indian Pediatr 1986; 23: 339-43.
21. Bhat IA et al. Perrinatal mortality in rural India (Chapt.4). Current trends in perinatal medicine Srinagar Ed. by N.A. Mir and M. Hassan Publ 1987 by Vishinath Press Srinagar p. 11-17.
22. Ramarao A. Some factors on perinatal mortality. Indian Pediatr 1970; 7:" 557-65.
23. Barros FC et al. Perinatal mortality in Southern Brazil a population based study of 7392 births. Bulletin of World Health Organisation 1987; 65(1): 95-104.
24. Gupta PK and Gupta AP. Perinatal mortality. Indian Pediatr. 1985; 22: 201-05.
25. Mohaptra SS. Rural perinatal mortality. Indian Pediatr. 1984; 21: 645-49.
26. Verma et al. Perinatal mortality in Ludhiana Punjab- A seven year hospital study. Indian Jr. of Paediatr 1992; 59: 561-65.
27. Thomas M. Collins et al. Value of perinatal interview in a perinatal mortality survey. Indian Jr. of Paediatr 1986; 53: 339-45.
28. Gopal S et al. Perinatal mortality in hospitalized deliveries (Chapt. 3). Current trends in perinatal Medicine Ed. by N.A. Mir and M. Hassan Publ. 1987, Vishinath Press Srinagar p. 11-17.
29. Nayak H Aum et al. Obstetric outcome in teenage pregnancy. Jr. of Obstet and Gynacol of India. Aug 1992; 42(4): 442-46.
30. Sanathana Krishan BR et al. Perinatal mortality in a referral teaching hospital in Madras city. Indian J. Pediatr. 1986; 53: 359-63.

With Best Compiments from

PARENTERAL DRUGS
(PUNJAB) PVT. LTD.

C & F Agents

medi-aid
agencies
1st. Floor, K.C. Plaza
RESIDENCY ROAD.
JAMMU TAWI (J&K.

Medi - Aid Agencies
K.C. PLAZA, RESIDENCY ROAD, JAMMU TAWI

Inguinal Hernia in Infants and Children in Kashmir, India

Shakeel A. Malik, MS, M.Ch; Rekha Patnaik, MS, M.Ch; Khurshid Sheikh, MS, M.Ch; Altaf Shera, MS;
Nisar A. Bhat, MS.

***Abstract:** Between January, 1987 and April, 1997 2892 children with inguinal hernia were operated upon in the department of paediatric surgery at Sher-i-Kashmir Institute of Medical Sciences, (SKIMS) Srinagar, Kashmir. 75% of the patients were below 5 years of the age and majority of the patients were boys (92%). There were (60%) right sided, 723 (25%) left sided and 434 (15%) bilateral hernias. Episodes of incarcerations occured in 4% cases. Only the symptomatic inguinal hernias were operated upon without a policy for contralateral exploration. Results following surgery were excellent.*

***Key Words:** Inguinal hernia, Incarceration, Contralateral exploration.*

JK-Practitioner 1999; 6(1): 46-47

Introduction

Indirect inguinal hernia is one of the most common surgical problems seen in infants and children. The incidence of inguinal hernia is reported to be 1% to 3% in fullterm babies and may be as high as 30% in prematures.[1,2] Episodes of incarceration occur in 6% to 18% cases. Puri et al noted a 31% incarceration rate in patients less than 1 year old.[3] The value of routine contralateral exploration has been debated because of the high incidence of testicular damage and negative explorations.[4]

Material and Methods

From January, 1987 to April 1997, 2892 children up to the age of 12 years were operated upon for inguinal hernia in the department of Paediatric Surgery. Their records were reviewed for clinical presentation, technique of surgery, policy of contralateral exploration and complication. The observations made in the present paper are based on the above work.

Results

The inguinal hernia was right sided in 60%, left sided in 25% and bilateral in 15% of cases; 98% were male and 2% female. 4% were admitted as emergencies for incarceration. Majority of the patients (60%) with incarcerated hernia were less than 1 year of age. 45% patients were under 2 years of age, 30% were between 2 and 5 years and remaining 25% were between 5 and 12 years of age. The youngest patient was 4 months and oldest 12 years of age. In cases of bilateral inguinal hernia, bilateral herniotomies were performed at one sitting. As a rule only symptomatic hernias were operated upon and routine contralateral exploration was not done.

Surgical procedure included high ligation of hernial sac using chromic catgut. Narrowing of deep ring was done in 15 cases. Post-operative complications included wound infection (10), scrotal haematoma (15) and recurrent hernia (5). Among the 5 recurrences, 2 were due to slipping of ligature while in remaining 3 no definite cause could be ascertained.

Discussion

Inguinal hernia repair is one of the commonest surgical procedure performed by paediatric surgeons. The reported incidence of inguinal hernia is 1-3% in full term babies and as high as 30% in prematures.[1,2]

All paediatric surgeons agree that an inguinal hernia should be operated upon as soon as possible after diagnosis. However, in our set up at SKIMS, due to long waiting period, surgery is often delayed for 2-8 months in uncomplicated cases.

The value of routine contralateral exploration is controversial. The advantage of contralateral exploration is that the child is spared a second operation. However, the herniotomy always carries a certain risk although small of injuries to vas, spermatic cord and posterior wall of inguinal canal. Moreover not all children with a patent processes vaginalis develop a symptomatic hernia requiring surgery.[4,5] At our Institution, as a rule we are operating only symptomatic hernias without contralateral exploration.

The incidence of recurrence varies from centre to centre. Causes of recurrence include slipped ligature,

From the Department of Paediatric Surgery, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India (Malik, Patnaik, Sheikh, Shera, Bhat)

Received April 1998 - Accepted November 1998

Correspondence to : Dr. Shakeel Ahmad Malik, 125 Magarmal Bagh, Srinagar, Kashmir-190009, (India)

tearing of sac, failure to ligate the sac high enough and injury to the posterior wall of inguinal canal.[6]

The incidence of recurrent hernia in our centre (0.2%), parallels the incidence reported in other series.[6,7] Inguinal hernia surgery in children is simple and if scientific principles are observed, is associated with excellent results.

References:

1. Coxja I. Inguinal hernia in childhood. Surg Clin North Am 1985; 65: 1331.
2. Harper RG, Garcia A, Siac. Inguinal hernia: a common problem of premature infants weighing 1000gms or less at birth. Pediatrics 1975; 56: 112.
3. Puri P, Guiney EJ, O'Donnel B. Inguinal hernia in infants: the fate of testis following incarceration. J Pediatr Surg. 1984; 19: 44-46.
4. Mc Gregor DB, Halverson K, Mc Vay CB. The unilateral pediatric hernia, should the contralateral side be explored? J Pediatr Surg. 1980; 15: 313.
5. Given JP, Rubin SZ. Occurrence of contralateral inguinal hernia following unilateral repair in a pediatric hospital. J. Pediatr Surg 1989; 24: 963-965.
6. Grosfeld JL, Minick K, Shedd F, West KW, Rescorla F, Vane DW. Inguinal hernia in children: factors affecting recurrence in 62 cases. J. Pediatr Surg 1991; 26: 283-287.
7. Zhang JZ, Li Xz. Inguinal hernia in infantrs and children in China. Pediatr Surg Int 1993: 8: 458-461.

JK-Practitioner

Get a

Free Copy

for your library

Make sure new ideas and information flow freely to your colleagues and students.

Complete and return the Library Recommenoation Form printed below, and we will send you a complimentary copy of **JK-Practitioner** for your institutional library.

To: Collections Development Librarian	**From:**
Name of Library ______________	Your name ______________
Name of institution ______________	Street address ______________
Street address ______________	City, State, Code ______________
City, State, Code ______________	

Comparative Evaluation of End Tidal Carbondioxide with Arterial Blood Gas Analysis

Anjum Basu; MD, Mehraj-u-Din, MD, FFARCS; Akhter Naqib, MD.

Abstract: The aim of this study was to evaluate the effectiveness and accuracy of Endtidal Carbon dioxide in different clinical settings. For this purpose 120 patients were taken and divided into two groups: In group-I minute volume was kept constant 15 ml/kg body weight and in group-II respiratory rate was constant 12 breaths per minute. It was seen that with constant minute volume and variations of respiratory rate there was a statistically significant change in PECO$_2$ and Paco$_2$, however, the difference between arterial and end-tidal Co$_2$ values was statistically insignificant. In group-II with constant respiratory rate 12 breaths/min, it was observed that the PECO$_2$ values showed a highly significant changes but the arterial to end-tidal Co$_2$ difference was statistically insignificant.

Key words:- Anaesthesia General Monitoring End-tidal Co$_2$, Arterial blood gas analysis.

JK-Practitioner 1999; 6(1): 48-50

Arterial blood gas analysis for Co$_2$ monitoring is an accurate and popular technique of documenting the adequacy of ventilation. It however has the disadvantage of being invasive, higher cost, risk of complication, represents only a discrete point in time and above all is not a continuous monitoring. All of these disadvantages can be obviated by the use of end-tidal Co$_2$ monitoring which is non-invasive, free of abnormalities that might be missed or delayed by reliance on arterial blood gas analysis alone. Some of the important uses of end-tidal Co$_2$ monitoring include early detection of misplaced tubes, air embolism, malignant hyperpyrexia, disconnection of the anaesthetic circuit in paralysed patients, reduction in cardiac output and the adequacy of muscle relaxation. This makes end-tidal Co$_2$ monitoring an attractive alternative to Arterial Blood Gas Analysis.

Material and Methods

120 patients (ASA-I) sixty of 20-40 years (group-I) and sixty of 60 years and above group-II either sex undergoing elective surgical procedures were studied.

Patients were given tab. diazepam 10mg orally as a sedative at bed time on the day prior to surgery and pre-medicated with intramuscular buprenorphine 5 micro gms/kg body weight one hour before surgery.

Anaesthesia was induced with STP 5 mg/kg body weight followed by suxamethonium 1.5 mg/kg body weight. After intubation anaesthesia was maintained with Nitrous oxide (76%) and O$_2$ and neuro-muscular block achieved with pancuronium bromide 100 micro gms/kg body weight.

Patients were ventilated with Siemen servo 900 "B" Ventilator and their Etco$_2$ was monitored with the help of Datascope Accucap monitor (side stream) and Siemens end-tidal Co$_2$ monitor. (main stream). No surgical intervention was allowed till the time the end-tidal Co$_2$ monitor displayed steady end-tidal Co$_2$ readings for at least a period of five minutes. After Allen's test to confirm the adequate collateral circulation, arterial blood samples was taken and immediately transported for Arterial Blood Gas Analysis in ice containers. Instant end-tidal Co$_2$ reading were recorded at the time the sample was with drawn. From the arterial and End-tidal Co$_2$ readings, arterial +o end-tidal Co$_2$ difference was derived.

For the purpose of study patients were divided into two groups of 60 each.

Group-I In this group minute volume was kept constant 15 ml/kg body weight and the influence of rate of change of ventilation on capnometry was observed (10 and 12 breaths/min). The observations were made in 2 sub-groups of patients.

Sub-group-I	20-40 years	(30 patients).
Sub-group - II	60 years and above	(30 patients).

Group-II In this group respiratory rate was kept constant 12 breaths/min. and the influence of change of minute ventilation 10ml/kg body weight and 15 ml/kg body weight was observed on copnometry. The observations were made in two sub-groups of patients.

Sub-group-I	20-40 years	(30 patients)
Sub-group-II	60 years and above	(30 patients).

From the Department of Anaesthesiology SKIMS, Srinagar, India (Basu, Prof. Mehraj, Naqib)

Received January 1998 Accepted November 1998

Correspondence to : Dr. Anjum Basu, C/o Dr. M.H.Basu, P.o Nehru Park, Boulevard, Gagribal, Srinagar-190 001, Kashmir (India)

Results:

Correlation of Etco$_2$ with arterial Pco$_2$ with constant minute ventilation (15 ml/kg body weight) and varying respiratory rate from 10 to 12 breaths/minute.

In the age group of 20-40 years, with constant minute ventilation (15 ml/kg body weight) and respiratory rate of 10 breaths/minute the mean PEco$_2$ (Date) was 29.63± 5.27 mm Hg while the mean PEco$_2$ (Servo) was 29.75±4.93 mm Hg. The mean arterial PCo$_2$ was 29.37±4.91 mmHg The mean arterial to end tidal difference was 0.12±0.45 mmHg (P>0.10) and 0.20±0.50 mmHg. (p>0.10) respectively with the Dates and Servo copnometers, which was statistically insignificant. However, when the respiratory rate was changed to 12 breaths/minute with constant minute ventilation (15 ml/Kg body weight) in the same group, their mean PEco$_2$ (Datex) was 27.35±5.52 mmHg. and PEco$_2$ (Servo) was 27.27±5.40 mmHg. The mean Paco$_2$ was 27.47±5.49 mmHg. The change in the CO$_2$ values caused by a change in the respiratory rate was statistically significant (p<0.01) with both Datex and Servo Copnomenters. The arterial to end-tidal Co$_2$ difference, however, was statistically insignificant (p>0.10).

In the age group of 60 years and above with constant minute ventilation (15ml/kg body weight) and respiratory rate as 10 breaths/minute, the mean PEco$_2$ (Datex) was 36.53±1.40 mmHg while the mean PEco$_2$ (Servo) was 36.29±1.44 mmHg. The mean -0.53±0.24 mmHg and -0.29±0.27 mmHg respectively with Datex and Servo Capnometers. This was statistically insignificant (p>0.20). However, when the respiratory rate was changed to 12 breaths/minute with constant minute ventilation (15ml/kg body weight) in the same age group, the mean PEco$_2$ (Datex) was 35.03±1.42 mmHg and PEco$_2$ (Servo) was 34.72±1.54 mmHg. The mean Paco$_2$ was 34.46±1.43 mmHg. The change in the Co$_2$ values caused by a change in the respiratory rate was statistically significant (p<0.01). The arterial to end tidal Co$_2$ difference was, however, statistically insignificant (p>0.20).

Correlation of Etco$_2$ with arterial Pco$_2$ with constant respiratory rate (12 breaths/minute) and varying minute ventialation from 10 ml to 15 ml/kg body weight.

In the age group of 20-40 years with constant respiratory rate (12 breaths/minute) and minute ventilation as 10ml/kg body weight, the mean PEco$_2$ (Date) value was 30-47±0.9 mmHg while the mean PEco$_2$ (Servo) value was 30.51±3.10 mmHg. The mean arterial Pco$_2$ was 30.81±2.95 mmHg with the arterial to end tidal difference being 0.34±0.33 mmHg (P>0.05) and 0.30±0.50 mmHg (p>0.20) respectively with Datex and Servo Capnometers. The arterial to end tidal Co$_2$ difference was statistically insignificant with both the Capnometers. However, when the minute ventilation was changed to 15 ml/kg body weight with constant respiratory rate (12 breaths/minute), in the same age group the mean PEco$_2$ (Datex) value was 27.72±3.01 mmHg and PEco$_2$ (Servo) value was 27.57±3.29 mmHg. The mean Paco$_2$ was 27.89±2.93 mmHg. The change in the Co$_2$ values caused by a change in the minute ventilation was statistically significant (P<0.01) with both Datex and Servo Capnometers. The arterial to end tidal Co$_2$ difference, however, was statistically insignificant (P>0.05) with Datex and (P>0.20) with Servo Capnometers.

In the age group of 60 years and above, with constant respiratory rate (12 breaths/minute) and minute ventilation as 10 ml/kg body weight the mean PEco$_2$ (Datex) was 37.23±1.26 mmHg while the mean PEco$_2$ (Servo) was 36.54±1.30 mmHg with the arterial to end tidal difference being 0.69±0.14 mmHg (P>0.20) and 0.17±0.44 mmHg (P>0.20) respectively with Datex and Servo Capnometers. The Arterial to End-tidal Co$_2$ difference was thus seen to be statistically insignificant with both the Capnometers. However, when the minute ventilation was changed to 15 ml/kg body weight with constant respiratory rate (12 breaths/minute) in the same age group, the mean PEco$_2$ (Datex) was 35.33±1.36 mmHg and PEco$_2$ (Servo) was 34.73±1.27 mmHg. The mean Paco$_2$ was 34.70±1.31 mmHg. The change in the Carbondioxide values caused by a change in the minute ventilation was statistically highly significant (P<0.001) The arterial to end-tidal Co$_2$ difference was however, statistically insignificant (P>0.20).

Discussion

The observations made with constant minute ventilation 15ml/kg body weight and varying respiratory rate from 10-12 breaths/minute in the age group of 20-40 years and 60 and above are in close agreement with those made by Engell and Ibsen (1951)[1]. These authors have reported that in steady state, the concentration of alveolar Co$_2$ is inversely proportional to the alveolar ventilation i.e. Hyperventilation causes a lowering while hypoventilation causes a rise of the alveolar Co$_2$ concentration. They have also remarked that alveolar and arterial Pco$_2$ approximate each other very closely and more so alveolar PCo$_2$, monitoring is quicker safer and very adequate for clinical use. Similar observations have been made by Jones et al (1979)[2] In their studies the PETCO$_2$ was found to predict Paco$_2$ to within 1.04 mmHG (±SD). The PECO$_2$-PaCo$_2$ was found to be inversely related to the frequency of respiration. The observation made in our study constant respiratory rate

(12 breahts/minute) and varying minute ventilation from 10 ml to 15 ml per kg. body weight are in agreement with those made by Nun and Hill[3] (1960) who have remarked that the mean arterial to end tidal Co_2 difference may be as much as 4.6±2.5 mmHg. Similar results have been reported by Jullian et al[4] (1990). They stated that in normal subjects, the Co_2 tension of end tidal respiratory gas closely approximate that of simultaneously drawn arterial blood, with a mean difference of 1.5±1.9 mmHg. Young and Robinson (1965) as quoted by Burton[5] (1966) have reported that an increase in the tidal volume leads to a decrease in the arterial to end tidal Co_2 difference. These observations are again in agreement with our study. Another study conducted by Whitesell et al (1981)[6] also show how closely peak expired PCo_2 reflects arterial PCo_2 during anaesthesia. The correlation between the two was significant ($1<0.0001$). These results are comparable to the results of our study. Takki[7] et al (1972) reported an excellent correlation between $Paco_2$ and $PECo_2$ during different rate and minute volumes of controlled respiration. The difference between the two has been reported to be of the order of 3.5 mmHg which are again in close agreement with the present study.

References:

1. Engell & N.C. Ibsen, B: Continuous Co_2 measurements in the respiratory air during anaesthesia in thoracic operations. Acta Scand 1955; 54:313-328.
2. Jones, NL; Robertson, D.G; Kane, JW; Difference between end tidal and arterial Pco_2 in exercise. Journal of Applied Physiology 1979; 47(5); 954-960.
3. Nunn, JF and Hill, DW, Respiratory dead space and arterial end tidal Co_2 tension difference in anaesthetized man. Journal of Applied Physiology 1960; 15: 383-387.
4. Jullian, DG; Travis DM, Robbin ED; Crump CA, Effect of Pulmonary artery occlusion upon end tidal Co_2 tension. Journal of applied physiology 1960; 15: 78-91.
5. Burton, BW. The value of Co_2 monitoring during anaesthesia. Anaesthesia 1966; 21: 173-183.
6. Whitesell, R; Assiddao, D.C; Gollman, D; Jablonski, J; Relationship between arterial and peak expired Co_2 Pressure during exercise and factors influencing the difference. Anaestheisa. Analgesia 1981; 60: 508-12.
7. Takki, S; Kauste A.K;. The validity and usefulness of the end tidal Pco_2 during anaesthesia. Ann: Clin: Res. 1972; 4: 278-84.

Seventh Annual Conference of National Academy of Burns, India, 5 to 7 February 1999 at Ahmedabad. For details contact Dr. P.K. Bilwani, Gujarat Burns Hospital, Opp. Tulsishyam Flats, Bhimjipura, Navavadaj Road, Ahmedabad 380 013.

Continuing Medical Education programme under the auspices of the Medical Council of India in consulting with the Ministry of Health and Family Welfare, Government of India and in collaboration with the Indian doctors residing abroad. **1. Nephrology,** 6 and 7 February 1999 at Varanasi. Contact the Organising Secretary, Dr. R.G. Singh, Professor and Head, Deparment of Medicine, Institute of Medical Sciences, Varanasi. **2. Pathology,** on 8 to 10 February 1999 at New Delhi. Contact the Organising Secretary Dr. P.Bajaj, Professor and Head, Department of Patholoty, Lady Hardinge Medical College, New Delhi.

CME in Diabetes and Endocrinology, 6 and 7 February 1999 at Tirupati approved for 5 RSSDI credit hours. Register by sending Rs. 350 by draft favouring CME on Diabetes too Dr. C.V.Harinarayan, Associate Professor and Head, Department of Endocrinology, Sri Venkateswara Institute of Medical Sciences, Tirupati 517 507.

V International Congress of Tropical Pediatrics, 10 too o15 February 1999 at Jaipur. For details contact the Secretary of the Organising Committee, Dr. Ashok Gupta, 25, Chetak Marg, M.D. Road, Jaipur 302 004.

45th Annual Conference of Cardio Vascular, Thoracic Surgeons - CT-CON 99, 23 to 26 February 1999 at Bhopal. For further details contact the Organising Secretary, Dr. S.S. Sharma, E-31, 45 Bungalows, North T.T.Nagar, Bhopal 462 003.

VIII Biennial National Conference of The Indian Society of Oncology, 12 to 14 March 1999 at New Delhi. For details contact Conference Secretariat, Batra Cancer Care Centre, Batra Hospital and MRC, 1, Tughlakabad Institutional Area, New Delhi 110 062.

JK-PRACTITIONER

Haemodyanamic, Biochemical and Haematological Profile during Transurethral Resection of Prostate:
A Comparison of the Effects of Glycine 1.5% and Distilled Water as Irrigating Fluid

Rukhsana Najeeb M.D; Imtiaz Naqash M.D.; Shigufta Qazi M.D; Abdul Qayoom Lone M.D.;
Mehraj-ud-Din D.A., FFARCS.

Abstract: The effects of glycine 1.5% and distilled water on haemodyanamic, biochemical and haematological parameters were compared in fifty patients undergoing transurethral resection of prostate (TURP). They were divided into two groups of twenty five patients each. In group I, 1.5% glycine was used as irrigating fluid while in group II distilled water was used as irrigating fluid. There was a significant decrease in heart rate in group II patients at 15 minutes and at completion of resection. Both systolic and diastolic blood pressures and central venous pressures (CVP) showed rise in group II patients at 5 and 15 minutes intraoperatively. Serum sodium levels decreased significantly in group II patients at completion of resection and 3 hours after completion of resection. A fall in serum chloride and bicarbonate levels were also observed at 3 and 24 hours after completion of resection in group II patients. Haemoglobin and haematocrit (PCV) values showed insignificant variation in both the groups and were within the normal range. The free plasma haemoglobin showed highly significant rise in group II patients at all the stages of resection. No clinical evidence of haemolysis or water intoxication was observed in either of the groups.

*Key words: Transurethral Resection of Prostrate (TRUP), Glycine, Distilled water,
Parameters: Haemodynamic, Biochemical and Haematologic.*

JK-Practitioner 1999; 6(1):51-53

Introduction

With the sophistication of endoscopes, TURP has become the treatment of choice in patients suffering from prostatic hyperplasia. To have an adequate and clear view of the prostate and to clear away the resected tissue, use of an irrigating fluid is mandatory. However the absorption of irrigating fluid is a potential hazard to patients undergoing TURP[1]. Such abosrption may lead to various symptoms often summarized as TURP syndrome, which include restlessness, chest pain, visual disturbances, nausea, vomiting, dyspnoea, hypotension and encephalopathy. The pathophysiological mechanisms of this syndrome include dilutional hyponatraemia and intravascular haemolysis[2]. Distilled water has long been used as an irrigating fluid during TURP, but increased incidence of water intoxication and haemolysis with it has restricted its use. Currrently the most commonly used irrigating fluid is glycine 1.5%. It is an ideal, iso-osmotic, non electrolytic and weakly ionised inexpensive irrigating fluid.

The present study was conducted to compare the effects of glycine 1.5% on haemodynamic, biochemical and haematological profile with that produced by distilled water used as irrigating fluid during TURP.

Methods:

Fifty patients of physical status ASA I and II scheduled for TURP were selected for this study. Patients with severe cardiac disease, bronchial asthma, hepatic and renal insufficiency and spinal anomalies were excluded from the study. Informed consent was taken from all the patients who were selected for this study. All the patients were premedicated with 10mg diazepam orally two hours prior to surgery. The patients were randomly allocated to two groups of twentyfive patients each. In group I, glycine 1.5% was used and in group II, distilled water was used as the irrigating fluid. In the operating room, after having established an intravenous line and fluid therapy started with Ringer lactate, patients were connected to Datex monitor for continuous monitoring of heart rate, ECG and non invasive blood pressures. Central venous pressure (CVP) was measured by water manometry after putting an EZ intravenous catheter through anticubital vein with the tip lying in the superior vena cava. All patients were administered spinal anaesthesia with 22G spinal needle at L3-4 space using

From the Department of Anaesthesiology & Critical Care Medicine, S.K. Institute of Medical Sciences, Srinagar-11, Kashmir, India. (Najeeb, Naqash, Qazi, Lone, Mehraj)

Received February 1998 Accepted November 1998

Correspondence to : Dr. Imtiaz Ahmad Naqash, Assistant Professor, Anaesthesiology & Critical Care Medicine, S.K. Institute of Medical Sciences, Srinagar-190011, Kashmir (India)

1.5 ml of 5% lignocaine hydrochloride. The haemodyanamic parameters (Heart rate, systolic blood pressure, diastolic blood pressure and CVP) were recorded pre operatively, 5 minutes, 15 minutes and at completion of resection of prostate. Venous blood samples for estimation of serum sodium, chloride, bicarbonate, haemglobin, haematocrit (PCV) and free plasma haemoglobin were collected pre operatively just before starting fluid therapy. Further samples were collected at completion of resection, 3 hours and 24 hours after resection. During the procedure, patients were continuously observed for clinical signs of water intoxication and haemolysis. The amount of irrigating fluid used, amount of tissue resected and time taken for resection was recorded. The data thus obtained was evaluated and analysed statistically using student's 't' test.

Result:

The mean age and weight of the patients, the amount of irrigating fluid used, time taken for resection and the amount of tissue resected are shown in tables I and II. Table III shows the haemodynamic changes in the two groups. As compared to group I, a highly significant fall in heart rate was observed at 15 minutes and at completion of resection in group II patients. A significant rise in both the systolic and diastolic blood pressures were observed in group II patients at 5 minutes and 15 minutes of resection. CVP also showed a rise at 5 minutes and at completion of resection in group II patients as compared to group I patients. There was a highly significant fall in serum sodium level at 3 hours and 24 hours after completion of resection in group II patients. Similarly serum chloride and bicarbonate levels showed highly significant fall in group II patients at 3 hours after completion of resection as compared to group I patients (Table IV). No variation of statistical significance was observed in haemoglobin and haematocrit levels in the two groups at different stages of resection. However the free plasma haemoglobin in group II patients showed a highly significant rise at all the stages of resection (Table V). There was no clinical evidence of haemolysis and water intoxication observed in either of the groups.

Table: I Mean age and weight of patients in the two groups.

Group	Age (years) Mean ± SD	Weight (kgs) Mean ± SD
I	77.08 ± 1.7	66.18 ± 3.33
II	74.0 ± 1.8	69.24 ± 4.10

Table : II Amount of fluid used, amount of tissue resected, and time of resection in the two groups

Group	Fluid use (litres) Mean ± SD	Tissue resected (Gms) Mean ± SD	Resection time (minutes) Mean ± SD
I	5.68 ± 1.23	18.0 ± 0.3	33.22 ± 1.33
II	7.32 + 1.44	22.0 + 0.5	44.50 + 10.8

Table : III Comparison of the haemodynamic changes between the two groups (Mean ± SD) at different stages.

Stage	Heart rate (Beats/min)		Systolic BP (MM Hg)		Diastolic BP (MM Hg)		CVP (Cm H_2O)	
	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II
Pre-op	90.72 ±9.80	94.04 ±4.08	112.44 ±4.95	115.60 ±6.51	80.00 ±11.18	77.92 ±8.13	3.21 ±1.67	3.21 ±1.67
5 Min. Intraop	91.88 ±8.33	83.04* ±11.75	113.60 ±15.85	129.12* ±20.48	77.80 ±7.51	94.16** ±14.46	3.69 ±1.60	3.94* ±1.60
15 Min. Intraop	93.28 ±7.56	80.74** ±11.75	117.54 ±16.41	136.56* ±19.82*	78.80 ±7.62	98.60** ±16.10	3.94 ±1.60	3.47 ±1.59
At Comp. of resection.	90.24 ±7.74	79.12** ±9.36	115.45 ±9.40	126.56* ±16.82	79.20 ±7.92	76.98 ±7.92	3.47 ±1.59	3.94* ±1.60

* Significant (P < 0.01)

** Highly significant (P (0.001)

Table : IV Comparison of the biochemical changes between the two groups at different stages. (Mean ± SD)

Stage	Sodium (mmol/L)		Chloride (mmol/L)		Bicarbonate (mmol/L)	
	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II
Pre-op	135.76 ± 6.19	136.12 ±7.15	97.96 ±10.26	98.56 ±9.25	23.68 ±2.43	23.08 ±2.56
At compl of resection	132.36 ±5.82	133.16 ±7.17	95.76 ±7.04	94.29 ±7.77	23.79 ±2.15	22.99 ±1.82
3hrs after resection	138.08 ±7.21	120.92** ±8.20	94.04 ±7.88	89.40 ±8.02	24.52 ±1.39	19.16** ±2.49
24 hrs after resection	134.68 ±6.86	126.80* ±11.44	96.96 ±9.15	94.48 ±11.03	24.44 ±2.16	20.08 ±1.98

* Significat (P <0.01)

** Highly significant (P<0.001)

Table: V Comparison of the haematological changes between the two groups at different stages. (Mean±SD)

Stage	Haemoglobin (gms/dl)		Haematrocrit (%)		Free plasma Hb (mgs/dl)	
	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II
Pre-op	12.16 ±1.97	13.25 ±1.92	37.09 ±8.74	37.09 ±8.74	1.66 ±0.86	1.24 ±0.83
At compl. of resection	11.90 ±1.97	12.00 ±2.02	35.63 ±5.30	35.96 ±5.32	4.42 ±1.98	29.24** ±21.59
3 hrs after resection	12.00 ±1.80	12.04 ±1.84	35.52 ±5.85	36.18 ±5.14	3.12 ±1.13	28.24** ±21.59
24 hrs after resection	12.52 ±0.58	12.26 ±0.58	37.20 ±5.41	37.92 ±5.50	1.16 ±1.28	12.68** ±10.56

**Highly significant (p<0.001)

Discussion:

Transurethral resectin of prostate which involves the opening of more than a few venous sinuses may lead to absorption of large quantity of irrigating fluid, the dangers of which have been recognised for many years[3,4]. The amount of absorption depends on the type of irrigating fluid used, hydrostatic pressure of the irrigating fluid, the number and size of open venous sinuses and the duration of exposure[5]. Distilled water by virtue of producing superior visibility was preferred for diagnostic procedures or resection of small amounts of tissue but its use was associated with increased incidence of water intoxication and haemolysis[6]. A variety of irrigating solutions have been used in a search for an ideal irrigating fluid to be used in TURP. One of the most commonly used irrigating fluid now is glycine 1.5% which has been shown to be an ideal irrigating fluid[7]. In our study we used glycine 1.5% and distilled water as irrigating fluid and compared their effects on haemodyanamic, biochemical and haematological profile. A highly significant fall in heart rate and rise in both systolic and diastolic blood pressures were observed in our patients who received distilled water as irrigating fluid as compared to glycine group. Our results are in accordance with that of Beal JL[8], who also found bradycardia and rise in blood pressure in 16% of their patients who received distilled water as irrigating fluid. Similarly a highly significant fall in serum sodium, chloride and bicarbonate was observed in our patients receiving distilled water as compared to glycine group. These values returned to near normal in 24 hours in both the groups. Such observations have been seen by many workers which are believed to be due to dilutional effect resulting from excessive intravascular absorption of irrigating fluid[9]. There was insignificant variation in haemoglobin and haematocrit values in both the groups at different stages of resection as compared to pre operative values, however a highly significant rise in free plasma haemoglobin seen in our patients receiving distilled water did not produce any clinical picture of haemolysis. This could possibily be attributed to following reasons:

i The patients included in our study were free from any renal disease and so were able to eliminate the free plasma haemoglobin without producing harmful effects.

ii The level of free plasma haemoglobin required to produce clinical picture of haemolysis is 3.7gm% which was never seen in our patients.

From our study it can be concluded that even though the complications with the use of glycine 1.5% as irrigating fluid have been reported yet its use is safe and has definite advantages over distilled water. Although no clinical evidence of haemolysis and water intoxication was seen in our patients, one should be aware of the complications that can occur as a result of the procedure and the use of irrigating fluid, and detect them promptly so that appropriate therapeutic measures can be instituted in time.

References:

1. Harrison RH, Boren JS. Dilutional hyponatraemic shock, another concept of TURP. J Urol 1956; 75: 95-110.
2. Rhymer JC, Bell TJ. Hyponatraemia following transurethral resection of prostate. British journal of urology 1985; 57: 450-452.
3. Creevey CD, Reiser MP. The importance of haemolysis in urethral prostatic resection: severe and fatal reactions associated with use of distilled water. J Urol 1963; 8: 900.
4. Thomas D, Hales P. Overhydration during Transurethral Resection of prostate using glycine as an irrigating solution. Anaesthesia Intensive Care 1984; 12: 366.
5. Fillman EM, Hanson OL, Gilbert LO. Radioosotopic study of effects of irrigating fluid in TURP. JAMA 1959; 171: 1488-1492.
6. Creevey CD. Haemolytic reactions during transurethral prostatic resection. J Urol 1974; 58: 125.
7. Desmond J. Complications of transurethral prostatic surgery. Canad. Anaesth. Society J 1970; 17: 25.
8. Beal JL. Consequences of fluid absorption during Transurethral resection of prostate using distilled water or 1.5% glycine. Canad. J Anaesthesiology 1989; 36:-3.
9. Still JA, Modell JH. Acute water intoxication during TURP surgery using glycine solution as irrigant. Anaesthesiology 1973; 38:1.

JK-PRACTITIONER

Double Blind Randomized Clinical Trial of a Herbal Formulation "Optiliv" in Acute Viral Hepatitis

N.R.Biswas, MD, DM; A. Vardhani, MD; P.K. Mongre, MD; A.Biswas, MD; R.M.Pandey, M.Sc, Ph.D.; A.K. Mathur, MD.

Abstract: *Viral hepatitis is a major public health problem in developing countries like India. It has emerged as a major cause of morbidity due to primary hepatic pathology in communities where public hygiene is poor. Considering the magnitude of the problem and the non-availability of suitable medication in the modern system of medicine, OPTILIV -a polyherbal formulation with known -hepatogenic and hepatoprotective actions was tried to alter the course of the disease and hasten recovery. Forty adult patients of either sex and between 14 to 50 years of age suffering from acute viral hepatitis were randomized. Optiliv capsules or placebo were given in 1 capsule B.D. dose for 15 days. Liver function tests and Hepatitis B Virus Surface Antigen determination was done before the trial and at monthly intervals. Three months follow up was done and improvement in clinical and biochemical recovery pattern was observed.*

Optiliv treated patients showed earlier clinical and biochemical recovery. Serum bilirubin values showed 50% decline much earlier (P<0.05). At the end of 8 weeks, SGOT (AST) and other biochemical values showed excellent recovery and reached normal levels while these values continued to remain higher in control group. There was no relapse in Optiliv treated group, while 2 patients had relapse in control group. Optiliv proved effective in treatment and faster recovery from acute viral hepatitis as shown by rapid clinical and biochemical improvements, without any relapse.

Key words: *Optiliv, Viral hepatitis, Herbal drug.*

JK-Practitioner 1999; 6(1): 54-57

Introduction

Viral hepatitis is a major public health problem throughout the world. Despite rapid advancement in modern medicine, there is no specific treatment for this disease. A number of plant products are claimed to be useful for treatment of liver disorders[1-3]. Optiliv is a polyherbal formulation containing hepatogenic, hepatoprotective and antioxidant herbs. Each 450mg capsule of Optiliv contains the standardized extracts of Andrographis paniculata -75 mg, Picrorrhiza kurroa -75 mg, Eclipta alba -75 mg, Boerhaavia diffuse -45mg, Azadirachta indica -30 mg, Swertia chirata -30 mg, Solanum nigrum -37.5 mg, Terminalia arjuna -15m, Apanamixis rohituka -15mg, Terminalia chebula -=30mg and Fumaria indica -22.5mg. The product was reported to be safe and non-toxic following long term administration in albino rats.[4] Hepato-protective action of Optiliv was reported both in-vitro and in-vivo models of experiments[5-6]. Phase -1 clinical trials confirmed the safety and tolerability of Optiliv in healthy human volunteers.[7]

No satisfactory treatment for viral hepatitis is available in modern medicine, till date. Anti-hepatitis vaccine against Hepatitis 'B' virus only is now available for prophylaxis but it is very expensive and provides protection for a limited period, hence it can not be used generally. There are many other viruses such as Hepatitis A, C,D, etc. which are commonly observed to cause viral hepatitis for which no vaccine is yet available. The incident of hepatitis 'A' virus infection is most commonly observed. Viral hepatitis is generally observed in India at the time of summer or rainy season when contaminated water becomes a source of infection. Therefore, it was decided to conduct a proper clinical trial, to assess the efficacy of herbal formulation OPTILIV in acute viral hepatitis.

Patients and Methods

Forty adult patients were randomized, after obtaining informed written consent. The clinical features observed on entry of these patients are summarized in Table 1.

From All India Institute of Medical Sciences, New Delhi, India (Biswas, Vardhani, Mongre, Biswas, Pandey) **and Envin Biocenticals Pvt. Ltd. Saharanpur (UP, India)** (Mathur)

Received September 1998 Accepted December 1998

Correspondence to : Dr. N.R.Biswas, Associate Professor, Deptt. of Pharmacology, Dr. R.P.Centre, All India Institute of Medical Sciences (AIIMS) New Delhi-110029 (India),
Ph.:6561123/Extn.362. Fax:91-11-6852919, Email: nrbiswas@medinst.ernet.in

The diagnosis of acute viral hepatitis was established from history, clinical examination and liver function tests. Exclusion criteria in this study were: duration of illness for more than four weeks, chronic alcoholism, age below 14 years and above 50 years, pregnancy, hepatitis precoma/coma and being under other hepatoprotective medications. The protocol was approved by the Ethical Committee. Treatment was started within 24 hours of admission. Optiliv was given in a dose of 1 capsule B.D. at one hour before meal for 15 days. If found necessary, a second course was advised. Although the recommended dose of Optiliv is 1 capsule O.D., in the present trial 1 capsule B.D. dose was followed due to the severity of the problem in acute viral hepatitis. Placebo capsules were administered in the same severity of the problem in acute viral hepatitis. Placebo capsules were administered in the same manner. No dietary restriction was imposed, but patients with severe anorexia and vomiting (4 on Optiliv, 7 on Placebo) were infused with intravenous glucose. Likewise, bed rest was not imposed. Vitamin K was administered to patients with prothrombin concentration less than 30% of normal, as estimated by prothrombin time (3 on Optiliv, 8 on placebo). No other durg except Vitamin B complex was allowed.

State of patients' well being, loss of appetite, presence of nausea, vomiting, fever, pruritis, rash, joint pain, abdominal discomfort, tiredness, colour of urine, hepatic enlargement and tenderness and liver function tests were assayed before starting treatment, twice in the first week and then at weekly intervals for next three weeks. Estimations of body weight, haemoglobin, serum bilirubin, SGOT, SGPT, Alkaline phosphatase, serum proteins, albumin and globulin were done initially and at the end of eight weeks.

Table-1
Clinical Features of Acute Viral Hepatitis Patients on entry (Mean±SD)

Features	OPTILIV (N=20)	PLACEBO (N=20)
Age (yrs)	32.5±4.2	33.6±4.2
Sex (M/F)	11/9	12/8
Weight (Kg)	59.3±2.7	53.7±4.1
Duration of illness (days)	13±7.1	15±8.2
Severity of illness (score)	12.3±2.8	13.8±3.2

Hepatitis B virus surface antigen (HbS Ag) was determined at the beginning and at monthly intervals. The clinical features were scored with the help of an arbitrary scoring system Viz, 0 (absent), 1 (mild), 2(severe). Side effects likely to be due to the treatment were also recorded. For those patients, who were discharged before the end of four weeks, evaluation was continued on a out-patient basis. The patients were followed up at monthly intervals for a total period of three months from the day of admission. The data was analyzed by student's t-test and Fisher's Exact test (for HbS Ag).

Results and Discussion

Table 2 outlines the results of the present study. Treatment with OPTILIV was associated with significantly less ($p<0.05$) loss in body weight and rapid ($P<0.05$) clinical recovery, as compared to placebo. Also there was a clear trend towards earlier biochemical recovery, as reflected by shorter time required for 50% decline in serum bilirubin levels ($P<0.05$) and normalization of SGPT levels ($P<0.05$). By the end of eight weeks, only 10 patients from placebo group recovered in contrast to 16 from OPTILIV treated group ($P<0.05$). As shown in Table-3 it is evident that in the Optiliv treated group, at the end of 8 weeks, SGOT (AST), SGPT (ALT) and Serum bilirubin showed excellent recovery and reached normal range at the end of 8 weeks though a downward trend was noticeable. This may be due to the self limiting nature of viral hepatitis as a disease. As mentioned above, clinical recovery was also hastened in the Optiliv treated group. Total proteins and alkaline phosphatase values were not significantly different in the Optiliv treated and placebo group. Two patients from placebo group had a replase of hepatitis (during 4th and 7th week respectively), from which they recovered uneventfully. No relapse was observed in Optiliv group. Side effects likely to be due to treatment were recorded in four patients on optiliv (diarrhoea, headache, epigastric pain, skin rash-1 case each), but the effect being transient, the discontinuation of the drug was not required. During follow up, four patients (all from placebo group) dropped out from the study at various time intervals.

Results of the present study showed earlier clinical and biochemical recovey in Optiliv treated patients. Serum bil;irubin values returned to normal earlier in Optiliv treated group. Choleretic action of Andrographic paniculata, picrorhiza kurroa and Boerhavia diffusa[11,17,19] may have caused better clearance of bilirubin through increased bile flow. Hepatogenic actions of the ingredients of Optiliv brought earlier clinical improvement. In comparaison to other commonly hepatoprotective herbal formulations; Optiliv contains standardized extracts of constituent herbs rather than crude powder or mass extracts. The use of standardized extracts ensures higher bioavialability of active constituents, for quick and sustained actions. Moreover, with the product thus being available in concentrated form, the dosage convenience for better patient compliance was achieved with 1 capsule twice daily dosage of Optiliv as against the dosage of several tablets, several times a day with other products.

Table-2

Response to Optiliv Treatment in Acute Viral Hepatitis (Mean±SD)

Parameters	OPTILIV (N=20)	PLACEBO (N=20)
Weight loss (kg)	1.2±0.8*	3.9±2.1
Time for clinical recovery (days)	17.1±1.6*	24.1±2.7
Time for 50% fall in Serum bilirubin (days)	9.8±1.4*	13.7±1.5
Time for Biochemical Recovery (days)	23.1±1.6*	27.4±6.9
Drop outs	0	4
HBsAG status	No change	No Change

*P<0.5

Optiliv contains the extracts of many internationally recognized herbs known for their hepatogenic and hepatoprotctive actions such as Eclipta alba, Picrorhiza kurroa, Andrographis paniculata, Boerhavia diffusa and Aphanamixis rohituka which are absent or used in negligible quantities in other formulations. Optiliv also contains herbs like Swertia chirata, Solanum nigrum and Azadirachta indica which are known for their digestive, enzymatic recovery from the symptoms of viral hepatitis and to restore normal digestive functions. It appears that the combined action of all the ingredients is responsible for beneficial results observed in this study.

Table-3

Comparison of blood biochemical parameters of patients with acute viral hepatitis in Optiliv vs Placebo group at the end of 8 weeks (values are Mean±SD)

Parameters	Placebo group	Optiliv Treated group	Significance
SGOT (AST) (IU/L) n=19	101.24±8.57	45.50±5.93	<0.0001***
SGPT (ALT)	99.03±10.30	50.25±5.84	<0.001***
Serum Bilirubin (mg/dl) n=20	1.29±0.15	0.90±5.84	<0.005*
Total Proteins (g/dl) n=20	5.61±0.42	5.69±0.27	NS
Alkaline Phosphatase (n=20)	130.16±6.17	104.52±3.90	NS

NS = Not Significant
*** = Highly significant
* = Significant

Looking to the encouraging results with Optiliv and high cost of anti-hapatitis vaccine, it may be useful to recommend OPTILIV as prophylactic in a dose of 1 capsule O.D. during summer and rainy season. Besides its hepatoprotective effect and keeping the liver optimally functional, it may also help in taking care of digestive disturbances, which are common in this period.

To summarize, administration of OPTILIV has proved beneficial in the treatment of acute vital hepatitis as indicated by rapid clinical and biochemical recovery, without any relapse in treated patients. It will be worthwhile to investigate its effects in other chronic hepatic disorders.

References:

1. Antarkar DS, Vaidya AB, Doshi JC, A double-blind clinical trial of Arogyavardhini-an Ayurvedic drug in acute viral hepatitis. Ind. J.Med. Res. 1988; 72: 588-593.
2. Blatter E, Caius JF and Mhaskar KS. Indian Medicinal Plants, 2nd Ed. Lalit Mohan Basu, Allahabad 1933.
3. Blum AL, Stuz R, Haemmerli UP. A fortuitously controlled study of steroid therapy in acute viral hepatitis. AM J Med. 1969; 47: 82-92.
4. Das SN and Chatterjee S Long term toxicity study of Optiliv. Indian J Ind. Med. 1995; 17: 61-81.
5. Das SN, Bansal N and CHatterjee S. Effect of Optiliv on Alcohol + Carbon Tetrachloride induced hepatotoxicity in albino rats. Indian J Ind. Med. 1995; 17: 27-3.
6. Veerendara KMH. Kidney tissue regeneration and kidney protective activity of LIVP-7 and ELKP-1 and hepatoprotective activity of LIVP-7 by in-vitro model. M Pharm (Pharmacology) thesis submitted to Govt. College of Pharmacy, Bangalore 1996.
7. Mathur AK, Chatterjee S, Agarwala SK and Jain AK. Safety and tolerability of Optiliv: a polyherbal formulation in healthy human volunteers. (Personal communication).
8. Gregory PB, Knauer CM, Kempson RL and Miller R. Steriod therapy in severe viral hepatitis: a double blind randomized trial of methyl prednisolone Versus placebo. N Eng. J. Med. 1976; 294: 681-687.
9. Dange SV, Patki PS, Bapat VM and Shrotri DS. Effect of Arogyavardhini against carbon tetrachloride induced hepatic damage in albino rats. Ind J Physiol. Pharma 1987; 31: 25-29.
10. Sama SK, Krishnamurthy L, Ramachandran K, Lal K. Efficacy of an indigenous preparation (Liv 52) in Acuteviral hepatitis- A double blind study. Ind. J. Med. Res. 1976; 64(5): 738-742.
11. Chaturvdi GN and Singh RH. Treatment of jaundice with an indigenous drug Picrorrhiza kurroa. Gurr. Med. Pract. 1965; 9: 451-461.
12. Chaturvedi GN, Tomar GS, Tiwari SK and Singh KP. Clinical studies on Dalmegh (Andrpgraphis paniculata nees) in infective hepatits. J. Int. Inst. Ayurveda. 1983; 2: 207-208.
13. Mehrotra R, Rawat S, Kulshreshta DK, Patnaik GK and Dhwan BN. In vitro studies on the effect of certain natural products against hepatitis -B virus. Indian J Med. Res. 1990; 928: 133-8.
14. Singh DS, Gupta SS, Ansari SA and Singh RH. A comparative study of Ayurvedic drugs Picrorrhiza kurroa (Kutaki) and Berberis aristata (Daruharidra) in acute viral hepatitis at Varanasi (India) J. Res. Edu. Indian Med. 1991; 10: 1-4.
15. Thyagarajan SP, Thiruneelakantan K, Subramaniaan S and Sunderavelu T. In-vitro inactivation of HBsAG by Eclipta alba, Hassak and Phyllanthus niruri Linn. Indian J Med. Res. 1982; 76 (Suppl): 124.

16. Srivastava S, Srivastava AK, Patnaik GK and Dhawan BN. Effect of andrographolide on liver regeneration in rats after partial hepatectomy (Abstract). Indian J Pharmcol. 19961 28:45.
17. Chandan BK, Sharma AK and Anand KK. Boerhavia diffusa: a study of its hepatoprotective activity. J. Ethnopharmacol. 1991; 31: 299-307.
18. Shukla B, Visen PKS, Patnaik GK and Dhawan BN. Choleretic effect of picroliv the hepatoprotective principle of Picrorrhiza kurroa. Planta Med. 1991; 57: 29-33.
19. Tripathi GS and Tripathi YB. Choleretic action of andrographolide obtained from Andrographis paniculata in rats. Phytother Res. 1991; 5: 176-8.

SUBSCRIBE

Subscription Rates
(India) in Rupees

	1 yr.	3 yrs.
Personal Rate	400	1000
Standard Rate	500	1200
Reduced Rate	250	x
Life Membership	**3000**	**10 Yrs**

Standard rate is for Institutions and Libraries
Reduced rate is for undergraduate students, interns and those under-going post graduate courses
Foreign

	1 yr.	3 yrs.
Gulf Countries	100 SR	275 SR
Rest of the World	$US 100	$US 200

JK-PRACTITIONER The International Journal of Current Medical Science & Practice

Name ____________________

Address ____________________

____

Institution/Hospital ____________________

Please tick box

☐ Yes send me JK-Practitioner

☐ Personal ☐ Standard ☐ Reduced

☐ I enclose a cheque/bank draft payable to the editor, JK Practitioner at Srinagar. (SBI, JK Bank or Grindlays Bank)

Expiry date ____________________

Signature ____________________

Date ____________________

Please return this order form to Dr. G.M. Malik, P.O.Box 884 GPO Srinagar 190 001 (Kashmir)

Testicular Pain in Acute Aortic Dissection

Showkat Bashir, MD; Riyaz Bashir, MD; Rashmikant Baxi, MD; Faroque A. Khan, MB.

Abstract: A 45 year old African-American male, previously healthy presented with severe, sharp retrosternal chest pain which was radiating to upper abdomen. He also complained of pain in his left testicle. On examination his blood pressure was 193/120 mmHg, equal in both arms with feeble pulses in lower extremities and had normal testicular examination. Transoesophageal echocardiography showed aortic dissection extending from just distal to left subclavian artery into abdominal aorta and aortogram confirmed aortic dissection upto left common itliac artery.

Key words: Dissection, Transoesophageal, False and true lumen, Radiation

JK-Practitioner 1999; 6(1): 58-59

Case Report:

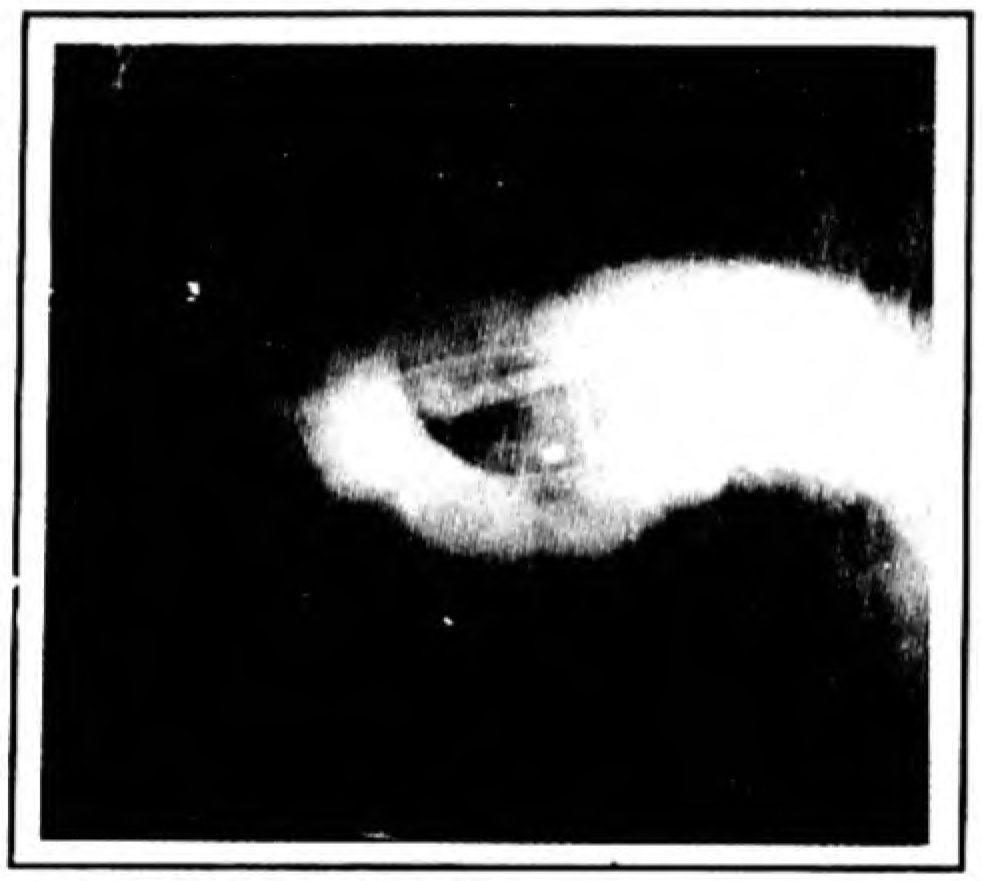


Fig1. Type III/B Aortic Dissection.
Thoracic Aortogram-Right-posterior-oblique projection. Injection into true lumen. False Channel is opacified, located posteriorly and on the left side. Dissection starting after left subclavian artery.

A 45 year old African-American male presented with acute onset, sharp rertrosternal chest pain which woke him up at midnight. The pain was radiating to upper abdomen and he also complained of severe pain in his left testicle. Pain was not relieved with intravenous nitroglycerin and had no postural variation. He denied any history of hypertension, diabetes, trauma, hypercholesterolemia, or any prior hospital admissions. On admission, the blood pressure was 193/120 mmHg, equal in both arms. However, pulse was feeble in right lower extremity and absent in left lower extremity. He had no marfanoid features. The heart sounds were normal and there was no evidence of aortic regurgitation. The abdominal examination revealed epigastric and left renal angle tenderness. Testicular examination was normal. His complete blood count, serum electrolytes, coagulation pofile, arterial blood gases and cardiac enzymes were all within normal limits. However his renal function tests showed elevated serum creatinine of 2.2meq/L. Electrocardiography showed rate of 68 beats per minute, normal sinus rhythm with non-specific ST and T wave changes. Chest roentgenogram showed mild cardiomegaly with no widening of mediastinum. The bed-side echocardiography showed moderate left ventricular hypertrophy, no wall motion abnormalities, no pericardial effusion, no valvular dysfunction and ejection fraction was 60%. The patients blood pressure was controlled with intravenous labetolol. Four hours later he developed gross hematuria.

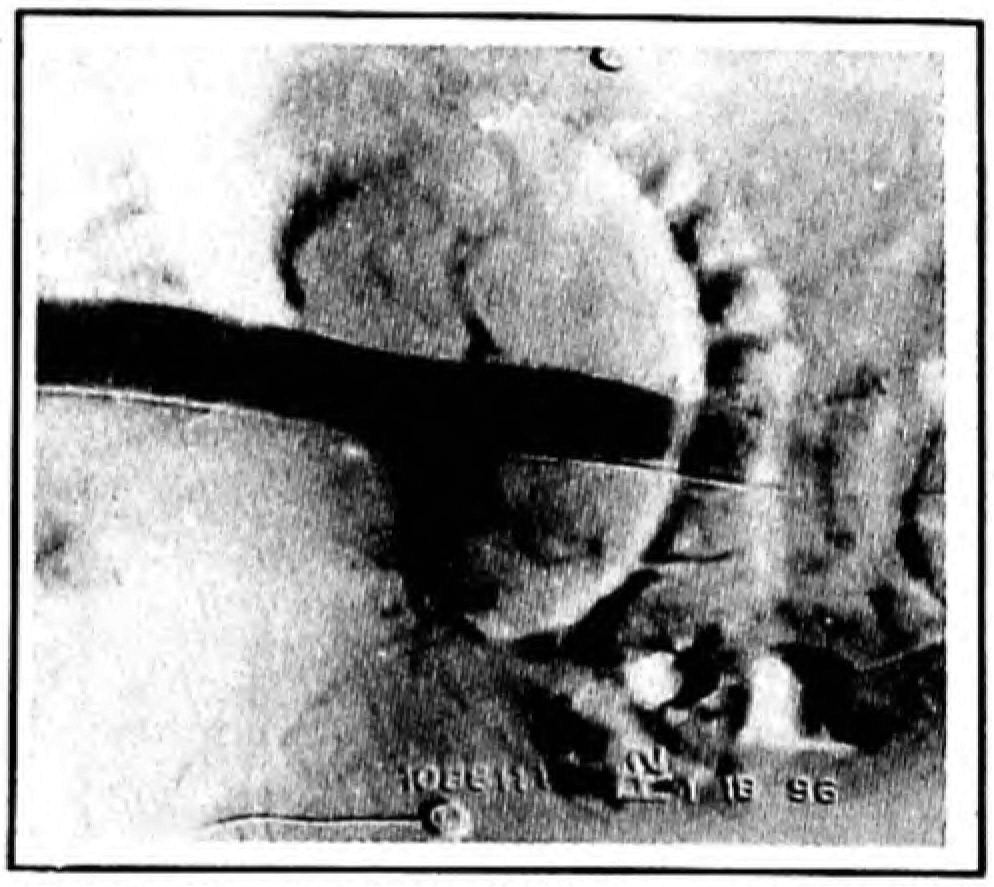


Fig 2. Low Thoracic and Abdominal Aortogram-Antero-posterior projection. False Channel large and is posterior and to the left. True lumen is narrowed and is on the right. False channel tapers and stops at L3. Celiac artery and superior mesenteric artery supplied from dilated false lumen. Right renal artery supplied by false lumen.

Transoesophageal echocardio-graphy showed aortic dissection originating just distal to left subclavian artery and extending into abdominal aorta. Aortography confirmed aortic dissection starting distal to left

---

From the Department of Medicine and Radiology, Nassau County Medical Center, State University of New York, Stony Brook (Showkat, Riyaz, Prof. Baxi, Prof. Khan)

Received April 1998 Accepted November 1998

Correspondence to : Faroque A. Khan, MACP MB, Chairman and Program Director, Department of Medicine, Nassau County Medical Center, State University of New York at Stony Brook, East Meadow, New York, NY 11554-1150, Tel (516) 572 6540 Fax. (516) 572 5609

subclavian artery and showing communication between false and true lumen (Fig.1). The dissection extended into the abdominal aorta, left common illiac, left external illiac artery and left common femoral artery (Fig. 2&3). Patient was also seen to have bilateral pelvic kidneys and renal arteries were arising from right common illiac artery. (Fig3).

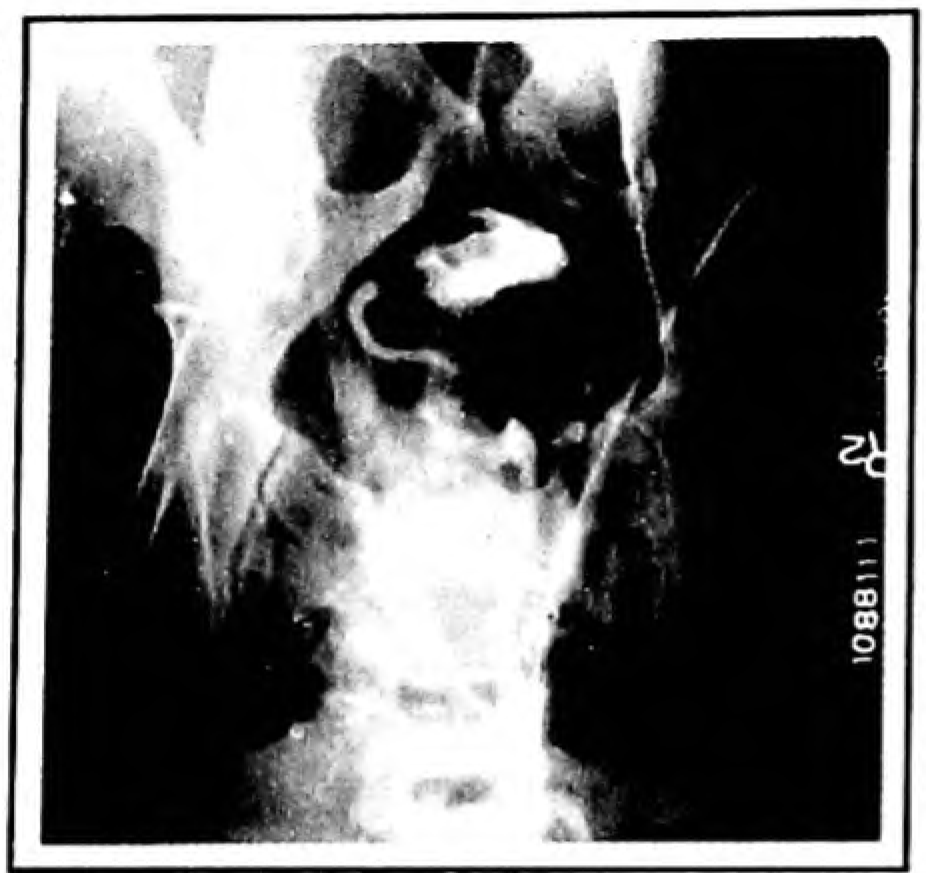


Fig 3. Pelvic Run-off-Anteroposterior View. Left Kidney low and situated in the right side of the pelvis, supplied by renal artery from right common illiac artery/true lumen. Dissection involves left common illiac, external illiac and left common femoral artery. True lumien on the right side.

Discussion:

Acute aortic dissections occur most frequently as a result of systemic hypertension; indeed it has been argued that if systemic hypertension was eliminated, spontaneous aortic dissections would virtually disappear[1]. Dissecting aneurysms are relatively rare in patients under forty except those with a familial predisposition, Marfan's syndrome, trauma, congenital heart disease such as coarctation of aorta and bicuspid aortic valve[2]. As many as 50% of dissecting aneurysms of the aorta seem to begin with medial degeneration followed by flexion stresses due to the repeated motion of aorta related to the beating of the heart[3]. Hydrodynamic forces in the blood stream related to acting upon the aortic wall cause the dissection to progress.

Almost all patients with acute aortic dissections present with pain. The pain is usually excruciating and may be described as sharp, knife-like or tearing in nature difficult to relieve with opiates. The pain is most often located in the anterior chest or in the back between shoulder blades and may radiate to upper abdomen or down along the spine, jaw or neck. Rarely dissections of lower thoracic aorta and abdominal aorta can occur without pain and present only as arterial insufficiency of legs. The perception of pain is believed to be carried by afferent sympathetic fibres while aortic dilatations and bleeding into surrounding tissues supposedly acts as a stimulus.[4]

Our patient, severely hypertensive on admission was found to have typical findings suggestive of aortic dissection. However, it was difficult to explain his testicular pain which clearly was not related to any inflammatory or traumatic condition even both clinically as well as historically. A careful search of English language medical literature did not reveal any association between aortic dissection and testicular pain, even though there were case reports of aortic dissection with wandering pains in lower abdomen[5]. The probable mechanism of this testicular pain in our patient may be either a referred pain or dissection extending into the testicular artery. The causal association of testicular pain with aortic dissection in our patient was substantiated by the fact that it got relieved with adequate management of his dissection.

Thus our case illustrates that in a patient with dissecting aortic aneurysm testicular pain may occur and, in fact, may provide a clue about the extent of dissection and this pain responds to adequate management of dissection. This case also illustrates that we need to closely look for ischemic damage to testes in patients with extending aortic dissections.

References:

1. Williams C. Roberts MD, Bethesda MD: Aortic Dissection; Anatomy, Consequences and Causes. Am Heart J; Feb 1981; 195-206.
2. Eric. W.Larson MD, William D Edwards MD: Risk Factors for Aortic Dissection; A necropsy Study of 161 Cases; Am J Cardiology 1984; 53: 849-855..
3. Wheat JR Med.Acute Dissecting Aneruysms of the Aorta: Diagnosis and Treatment -1979. Am Heart J; Mar 1980; 99, No. 3:373-386.
4. Stafford Cohen MD, David Littma MD: Painless Dissecting Aneurysm of the Aorta. N Engl J Med; 1955, 271, No. 3, 143-45.
5. Weiss P. Actue Aortic Dissection. Ther Umsch 1995; Mar; 52(3):165-9.

Compensatory Hypoventilation with Hypercapnia in Metabolic Alkalosis in a Patient with Gastric outlet Obstruction-A Unique Case Report

Musarat Shareeff, M.D.; Showkat Bashir, M.D., Faroque A. Khan, M.B., M.A.C.P.

Abstract: *Hyperventilation is a well-known compensatory physiological mechanism in metabolic acidosis. On the other hand, compensatory hypoventilation in metabolic alkalosis has rarely been reported, even though recent literature suggests that it may be a relatively common occurrence*[1,2]. *This hypoventilation may result in a variable clinical picture, with features of underlying alkalosis. It is important to recognize this phenomena clinically with its accompanying metabolic derangements, even though they usually resolve spontaneously. We report a case of severe metabolic alkalosis secondary to protracted vomiting due to gastric outlet obstruction, causing hypoventilatioon and hypercapnia. The patient's condition improved with treatment of metabolic alkalosis.*

Key words: *Hypoventilation; Hypercapnia; Metabolic Alkalosis and Acidosis*

JK-Practitioner 1999; 6(1): 60-61

Case Report

A 38-year old African-American male was admitted with upper abdominal pain and protracted vomiting of three-days duration. His past medical history was significant for duodenal ulcer complicated by pyloric stenosis, which was being managed medically. There was no history of fever, gastrointestinal bleeding, diarrhea, jaundice, anorexia, or weight loss.

On physical examination he was alert, but drowsy, with an emaciated look. His vital signs showed a pulse of 80/min, blood pressure of 100/60 mmHg with no change in pressure in the sitting position, respiratory rate of 12/min. He was afebrile. No pallor or icterus was noted. The chest and cardiovascular examinations were unremarkable. The abdominal examination showed mild epigastric tenderness with no guarding or rebound. There were no visible peristalsis or any succussion splash. No ascitic fluid was detected and bowel sounds were normal. The rectal examination was normal.

The laboratory data showed hemoglobin and hematocrit of 13 gm% and 38%, respectively. The serum electrolytes revealed sodium of 133 meq/l (normal: 140-144 meq/l), potassium of 3.0 meq/l (normal: 3.5-4.5 meq/l), Bicarbonate of 41 mmol/l (normal: 25-30 mmol/l) and chloride of 70 meq/l (normal: 90-100 meq/l). The blood urea and nitrogen was 46 mg% (normal: 15-20 mg%), while as serum creatinine was 3.6 mg% (normal: 0.5-1.5mg%). The liver function tests, amylase, lipase, and albumin were within normal limits. The arterial blood gas analysis done on room air showed pH of 7.54, PCO_2 of 54.6 mmHg and PO_2 of 61.8 mmHg. The routine urinalysis was normal. The chest radiograph, electrocardiogram, and ultrasound of kidneys were normal. The abdominal plain films revealed no free air or any signs of obstruction. The repeat esophagogastroduodenoscopy confirmed beingn gastric outlet obstruction with mild esophagitis.

He was started on intravenous hydration with normal saline along with nasogastric suction for bowel rest. He received parental H_2-blockers and antiemetics. He began to improve within next two days when his conscious state returned back to normal. His electrolytes and renal function also normalized with appropriate volume replacement (Table 1). During the hospital course his blood pH and PCO_2 continuously improved without any extrinsic respiratory support. The patient was advised surgery for his pyloric stenosis but was lost to follow up.

Discussion

Hyperventilation is a well-known compensatory mechanism in metabolic acidosis, and the consistent relationship between PCO_2 and plasma bicarbonate during the steady state indicates a highly predictable degree of respiratory compensation[1,3,4]. On the other hand, respiratory compensation (hypoventilation) in metabolic alkalosis has been inconsistent and controversial. However, recent studies invariable cite

From Department of Medicine, Nassu Countsy Medical Centrė East Meadow, NY (Shareeff, Bashir, Porf Khan)
Received October 1998 Accepted December 1998
Correspondence to : Dr. Musarat Shareeff, M.D. Department of Medicine Nassau Country Medical Center 2201 Hempstead Turnpike East Meadow, NY 11554

appropriate hypoventilation in the setting of metabolic alkalosis, and it is believed that there is a general lack of reporting of such cases[1,2,3]. The rarity of such cases is attributed to the presence of the other disorders accompanying metabolic alkalosis-like hypokalemia, hypoxemia, ad azotemia, which may account for the lack of appropriate hypoventilation in this disorder.

Table-1:

Day	pH	PaCO$_2$ (mmHg)	PaCO$_2$ (mmHg)	Na (meq/l)	K (meq/l)	HCO$_3$ (mmol/l)	Cl (meq/l)	BUN (mg/dl)	Cr (mg%)
1	7.54	61.8	54.6	133	3.0	41	70	46	36
2	7.62	67.0	54.0	133	3.4	38	82	52	3.2
5	7.44	101.	47.8	137	4.1	27	102	24	1.8

The Hypoventilatin associated with metabolic alkalosis was believed to be secondary to hypokalemia, causing respiratory muscle weakness[2]. However, experimentally induced metabolic alkalosis and hypokalemia neither causes nor prevents hyp-ventilation. Similarly, hypoxemia does not increase the ventilatory drive probably secondary to blunted response of peripheral chemoreceptors to low oxygen in metablic alkalosis[1]. In addition, azotemia was supposed to be a contributing factor for hypoventilation, but recent studies have shown hypercapnia in the absence of azotemia in metabolic alkalosis[3,4]. The ventilatory change is believed to be noticed only once bicarbonate levels increase beyond 40 mmol/l, as was observed in out patient[1,2,3,4]. The possible explanation as to why hypoventilation becomes evident only once bicarbonate levels increase beyond 40 mmol/l is: In mild or acute metabolic alkalosis, bicarbonate combines with H in plasma and increase the plasma PCO$_2$, which rapidly equilibrates with brain tissue PCO$_2$ and causes a fall in brain interstitial fluid pH, consequently stimulating ventilation. As time passes, or servere metabolic alkalosis persists, alkalosis prevails in both blood and brain-hence, reduction in brain H resulting in raised pH and blunted ventilatory rate[2,6]. It is also suggested that reduced ventilatory drive in metabolic alkalosis may be because of diminished peripheral chemoreceptor drive to ventilation without a significant depressant effect becuase of an alkaline CSF pH.[6]

Our patient was admitted with hypochloremic metabolic alkalosis with azotemia, mild hypoxemia and hypercapnia. His clinical condition improved following the restoration of his fluid deficit, and led to correction of his alkalosis, with resolution of hypercapnia. The extensive search of English medical literature did reveal serveral cases of compensatory hypoventilation in metabolic alkalosis due to diuretic usage, staravation, etc. Howere, our case is only the second one in which gastric outlet obstruction was responsible for metabloic derangements and hypoventilation[5].

We believe that hypoventilation with hypercapnia is a definite compensatory response to metabolic alkalosis, especially in severe cases. The resultant hypercapnia, once correctly identified as an appropriate compensation for metabolic alkalosis, can easily be managed with treatment of the primary process; i.e., metabolic alkalosis.

In conclusion, this brief case report highlights: a) that in severe metabolic alkalosis, with bicarbonate levels greater than 40 mmol/l, hypoventilation as a compensattory mechanism is a rule rather than an exception; b) the rise of PCO$_2$ should not be interpreted too represent acute respiratory failure, and c) therapy should be directed towards elimination of the primary process; i.e., metabolic alkalosis.

References:

1. Javaheri S, Kazemi H: Metabolic Alkalosis and Hypoventilation in Humans. Am Rev Resp Dis 1987, 136:1011-1016.
2. Blank MJ, Lew SQ: Hypoventilation in a Dialysis Patient with Severe Metabolic Alkalosis -Treatment by Dialysis. Blood Purif 1991; 9:109-113.
3. Fulop M: Hypercapnia in Metabolic Alkalosis. NY State J Med 1976; 19-22.
4. Tuller MA, Medhi F: Compensatory Hypoventilation and Hypercapnia in Primary Metabolic Alkalosis. Am J MEd 1971, 50:281-290.
5. Lavie et al: Marked Hypochloremic Metabolic Alkalosis with Severe Compensatory Hypoventilation Southern Med J 1986, 79(10): 1296-1299.
6. Javaheri et al: Compensatory Hypoventilation in Metabolic Alkalosis. Chest 1981, 3: 1982, 296-300.

Patent Ductus Arteriosus in Sister and Brother with Congenital Hydrocele

M.A. Kamili MD; S.A. Kadla MD; H.A.Khan; A. Gani MD; P.A. Shah MD; N.A. Bhat MD;
N.A. Lone M.B.B.S.; A. Nafae MD.

Abstract: *We are reporting a family where a brother and his sister had patent ductus arteriosus in the family under report two cousins had congenital hydrocele, one having it in association with PDA.*

Key words: *Patent ductus arteriosus, Congenital hydrocele, Association.*

Abbrevations: *PDA (Patent ductus arterosus), PAH (Pulmonary arterial hypertension), MVP (Mitral value prolapse)*

JK-Practitioner 1999; 6(1): 62-63

Introduction:

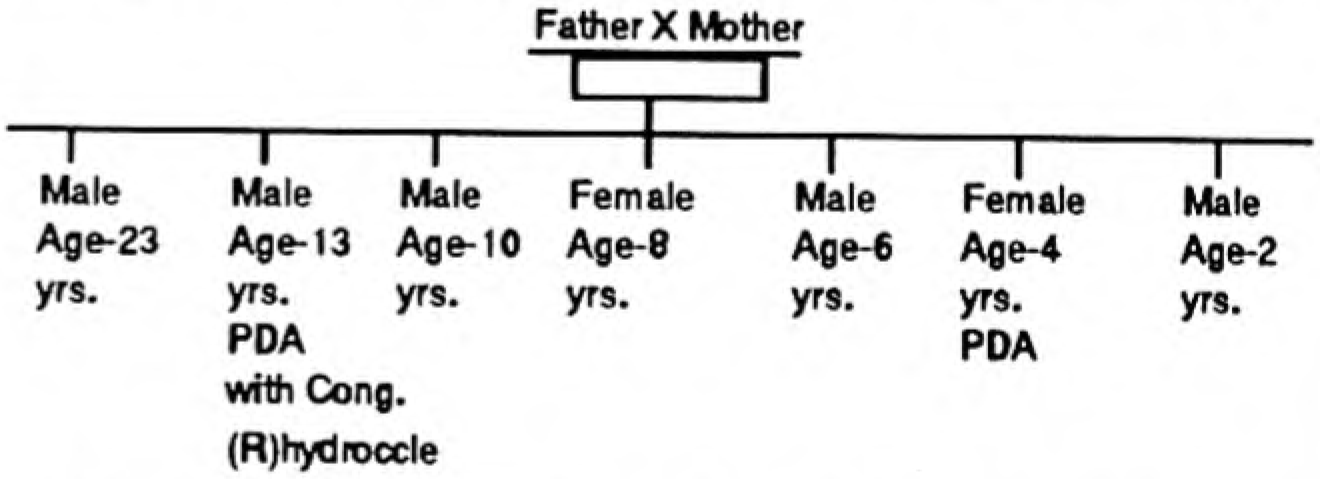
Patent ductus arteriosus (PDA) is an abnormal persistance of a normal foetal vasular channel between the pulmonary artery and aorta. The incidence of patent ductus arteriosus is appoximately 1 in 2000 live births i,e., about 10% of all varieties of congenital heart disease[1] PDA may be present either alone or in combination with other congenital cardiac disease like pulmonary atresia with intact ventricular septum, aortic atresia, transposition of great vessels and etc. PDA has been reported to occur as a result of many conditions like genetic disorder, chromosomal disorders and teratogenic effects.[2] However association of familial PDA with familial congenital hydrocele has not been reported so far to best of our knowledge.

Case Report

A 13 year old boy born of non consanguinous marriage was brought to our hospital with the history of swelling of right testis which was present since his birth. Initially the swelling was of small size and as the age progressed, it also increased in the size till it reached present size. There is history of temporary increase in the swelling whenever child used to cry. There was no history suggestive of Rubella infection or drug intake by his mother during pregnancy. The child was born of a full term normal delivery with normal birth weight and mile stones. Excessive movements of his chest had been noticed by his parents since his childhood. The examination revealed patient of average built with normal pulse and blood pressure, mid arm and head circumferences. In addition his height, growth and mental development, eyes, were normal. There was no clubbing or cynosis. The examination of chest revealed significant precordial movements with visible pulsations in the left IInd intercostal space. The rest of the examination of chest was normal. The examination of CVS revealed cardiac apex in the 5th intercostal space, just out side mid-clavicular line. There was a systodiastolic thrill in the left parasternal area in the IInd space on auscultation there was a continous machinery murmer heard in the left IInd intercostal space close to lateral sternal border.

The IInd heart sound was totally drowned by the murmer. The examination of abdomen revealed right scrotal swelling with positve cough impulse and positive transillumination test. Thus a clinical diagnosis of congenital acynotic heart disease in the form of PDA with PAH (left to right shunt) and right congenital hydrocele was putforth.

There was a history of perception of similar chest movement by their parents in younger sister of the patient. The clinical examination of the child revealed, she too having a PDA without PAH (L-R shunt). The family tree of these patients is depicted as under (Fig.I)



Both subjects were investigated, Haemogram, Urine examination, LFT, KFT, examination of the fundi was normal. ECG revealed in both cases large mid precordial complexes.

The x-ray chest (PA view) in the male patient revealed

From the Department of Medicine, GMC, Srinagar, Kashmir, India (Kamili, Kadla, Khan, Gani, Shah, Bhat, Lone, Prof. Nafae)

Received September 1998 Accepted November 1998

Correspondence to : Dr. M.A. Kamili, 52-Balgarden, Srinagar, Kashmir, India - 190 010

LV type cardiomegaly while as in the female patient x-ray chest (PA view) was normal. The echocardiogrphy in male patient was consistant with PDA with mild MR due to Mitral Valve prolapse (non-Rheumatic) and PAH. While in case of female patient it was consistant with PDA without PAH.

Discussion

The PDA is known to occur in families. There is often recurrence in siblings[3,4,5,6]. In the present case we examined all first degree relatives of the patient and their parents. In total there were about 40 children who had normal cardiovascular examination. There was only one boy (Paternal cousin age 11 years) who had right congenital hydrocele with left varicocele and vitiligo patch on left leg. Another male member who was the paternal nephew (age 23 years) of the patient had alopacia totalis which had occurred during his seventh year of life after taking some drugs. The nature of these drugs was not known. Despite exhaustive scanning of literature, we could not come across even a single case report in which congenital hydrocele was associated with familial PDA. To project it as a simple coincidence is not justified and a possible familial association of hydrocele and PDA with variable penetration can not be ruled out.

References:

1. Cargren, L.E: The incidence of congenital heart diseases in children born in Gothenburg 1941-45, Br. Heart Journal 1959; 21:40.
2. Villiam F. Friendman, Eugene Braunwald, Heart diseases; a Text book of Cardiovasular Medicine, 4th edition 1992. W.B. Saunders., P878-965.
3. Anderson, R.C, Adms, P.Jr. and Varco, R.L. Patent ductus arteriosus with reversal of flow. Clinical study of 10 children, Pediatrics 1956; 18:410.
4. Bonlay, R.J. Patent ductus arteriosus in identical twins. American J. Cardiology 1961;7:270.
5. Burman, B, Familial patent ductus arteriosus. Br. Heart Jr. 1961;23:603.
6. Joycee, J.C. and O'Toole, S.P: Congenital heart diseases. Report of an unusually high incidence in one family. Br. Med. Jr. 1954; 1:1241.

DECLARATION UNDER SECTION 5 OF THE PRESS AND REGISTRATION BOOKS ACT OF 1967 AS AMENDED FROM - I (SEE RULE I)

1. Title - **JK-PRACTITIONER**
2. Place of publicaton - Srinagar
3. Periodicity of publication - Quarterly
4. Publisher's name - Dr. G.M. Malik
   Whether Citizen of India - Yes
   Address : Jhelum Market, Batmaloo, Srinagar - 190 010, Kashmir (India)
6. Editor's Name - Dr. G.M.Malik
   Citizen of India - Yes
   Address : Jhelum Market, Batmaloo, Srinagar - 190 010, Kashmir (India)
7. Particulars of other individuals who are owners/share holders of Newspaper.

I Dr. G.M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

Sd/-

Dr. G.M. Malik

An Unusual Cause of Dysphagia - A Large Cervical Osteophyte

N.Bharadwaj; MBBS MS; V.P. Venkatachalam, MS, FICS, FIMSA, FIAMS, DLO

Abstract: A case of dysphagia due to large cervical osteophyte and role of conservative and surgical treatment has been discussed.

Keywords: Dysphagia, Osteophyte

JK-Practitioner 1999; 6(1): 64-65

Introduction

Dysphagia which means difficulty in swallowing can be due to a variety of causes i.e. Malignancy of hypopharynx or oesophagus, oesophageal webs, spasm or incoordination of cricopharyngeal muscle, stricture of oesophagus, gastrooesophageal reflux, neurological and neuromuscular disorders. Although cervical spine disease is very common but dysphagia due to cervical spine disease is very rare. Till now more than 40 cases of dysphagia due to cervical spine disease have been reported. A case of dysphagia due to anterior cervical giant osteophyte is reported.

Case Report

A 54 year old male farmer presented with difficulty in swallowing for last 6 months which was gradually progressive in nature. This difficulty was for solid foods only. He had to take liquids along with solids to pass the bolus down. He denied any history of trauma, weight loss, choking spells, haematemesis or hemoptysis, or use of medications. There was no history of waterbrash or epigastric pain or retrosternal pain.

On general physical examination no abnormality was detected.

On examination of oral cavity and oropharyn mild hyperaemia of posterior pharyngeal wall was noted. On indirect laryngoscopy, base of tongue and valeculla were normal. Epiglottis was slightly thickened. Pharngoepiglottic, aryepiglottic folds, false cords and true cords were normal. Both cords had normal mobility. Both the arytenoids were slightly congested and oedematous. No pooling of saliva was seen in either pyriform sinus. No growth was seen in laryn Anterior and posterior rhinoscopic findings did not show any abnormality.

Routine haematological and urine investigation were normal.

X-ray chest PA view showd only prominence of bronchovascular markings. Cardiac size was normal and there was no mediastinal widening or hilar lymphadenopathy. X-ray cervical and soft tissue neck lateral view showed evidence of minimal ankylosis with hyperostosis. Prevertebral soft tissue shadow was of normal width.

Barium swallow was done which surprisingly showed indentation of Barium column at lower end of C6 by a large anterior cervical osteophyte which could be clearly observed in the radiograph.

Flexible fibre optic oesophagoscopy was done and a smooth swelling was encountered with surrounding edema and congestion just below the cricopharynx. Oesophagoscope was not passed below this level due to danger of oesophageal perforation.

After making a diagnosis of extra-luminal compression of oesophagus just below cricopharynx by a large osteophyte he was treated conservatively with anti-inflammatory agents and steroids and antiacids but showed very little improvement in dysphagia.

Finally surgical excision of the osteophyte was carried out by using standard lateral cervical approach. Patient improved dramatically and was symptom free 48 hrs. after surgery when he was allowed semisolid food. He was followed up for two years and till now he is symptom free. Repeat barium swallow showed normal study.

Discussion

In the evaluation of dysphagia a large number of causes have to be kept in mind which include malignancy, oesophageal webs, stricture, etc. Normally diagnosis of globus hystericus is made when no obvious cause can be established . In majority of globus hystericus cases neuro-muscular cause of dysphagia has to be ruled out. In such elderly cases disease of cervical spine should be looked for, since cervical osteophyte formation or

From the Department of Otorhinolaryngology Safdarjung Hospital (Bharadwaj, Venkatachalam) New Delhi, India
Received October 1997 Accepted September 1998
Correspondence to : Dr. N.Bharadwaj, 1029, Sector-8, R.K.Puram, New Delhi

ankylosing hyperostosis may be cause of dysphagia[1].

It has been postulated that intervertebral disc degeneration and anterior herniation results in proliferation and metaplasia of inner annular fibres into cartilage. Further calcification, ossification and traction of spinal muscles results in osteophyte formation[2].

Another form of disease is called Ankylosing vertebral hyperostosis or Foresitier's disease which may be the cause of dysphagia. In this disease bony bridges unite the ventral aspects of contiguous vertebral bodies. There is no disc degeneration associated. The pathology in this disease is related to linear ossification of anterior spinal ligament. Large osteophytes of the spine are usually observed in diffuse idiopathic skeletal hyperostosis (DISH) or Foreistier's disease. Various authors have reported cases of dysphagia due to DISH termed as DISHphagia[3,4,5,6,7]. It has been said that 17% of Foreistier's disease have dysphagia. Dysphagia due to large osteophyte is mainly due to mechanical obstruction or its secondary effects. If the osteopyhyte is very large (as in our case) it will cause mechanical extraluminal obstruction. This obstruction is more troublesome if it is at places where the oesophagus is anchored i.e. at cricoid cartilage level and diaphragm. It is also reported that there is inflammation and surrounding oedema in the viscinity of osteophyte which is the cause of dysphagia. Therefore, anti-inflammatry agents and steroids should be tried in less severe cases. Surgical treatment is indicated in cases who do not improve with conservative treatment.[8]

References:

1. Lambert JR, Teperman PS, Jimenez J, Newman A: Cervical spine disease and dysphagia, Four new cases and review of literature, Am J Gestroentrol 1981; 76: 35-40.
2. Lipson SJ, Muir H: Vertebral osteophyte formation in experimental disc degeneration, Arthritis Rheum 1980; 23:319-324.
3. Blumberg P, Prapot C, Viscomi G: Cervical osteophytes producing dysphagia, Ear Nose Throat 1977; J56-396.
4. Bone R C, Natium A M, Harris A S: Evaluation and correction of dysphagia producing cervical osteophytosis, Laryngoscope 1974; 84:2045.
5. Gobel VK, Karasick S, Canino C: Cervical spondylotic dysphagia, JAMA 1976; 235: 935.
6. Ratnesar P: Dysphagia due to cervical eostosis, Laryngoscope 1970; 80:496.
7. Sounders W H: Cervical osteophytes and dysphagia Ann. Ottol. Rhino. Laryngol 1970; 79: 1091.
8. Hirano H, Suzuki H, Sakakibara T, Higuchi Y, Inove K, Suzuki Y: Dysphagia due to hypertropic cervical osteophytes, clin Orthop 1982; 167: 168-172.

Chromosome Study in a Child with Ambiguous Genitalia

S.C.Gupta; H.L.Goswami; TR Raina

Abstract: Chromosome study in a 2½ yrs, old child with Ambiguous genitalia is reported. Beside sex-chromosome mosaicism (45, X/46, XY), the structural abnormalities like ring-chromosome and telomeric associations among some of the chromosomes have also been recorded and held responsible for the death of the proband in infancy.

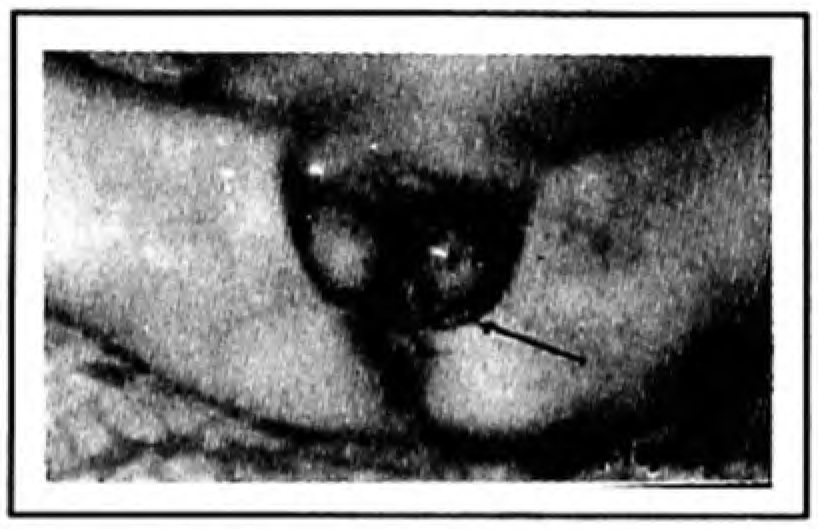
Key Words: Ambiguous genitalia, Bifid scrotum, Sex-chromosomes mosaicism, Ring chromosome, Telomeric associations.

JK-Practitioner 1999; 6(1): 66-67

Introduction:

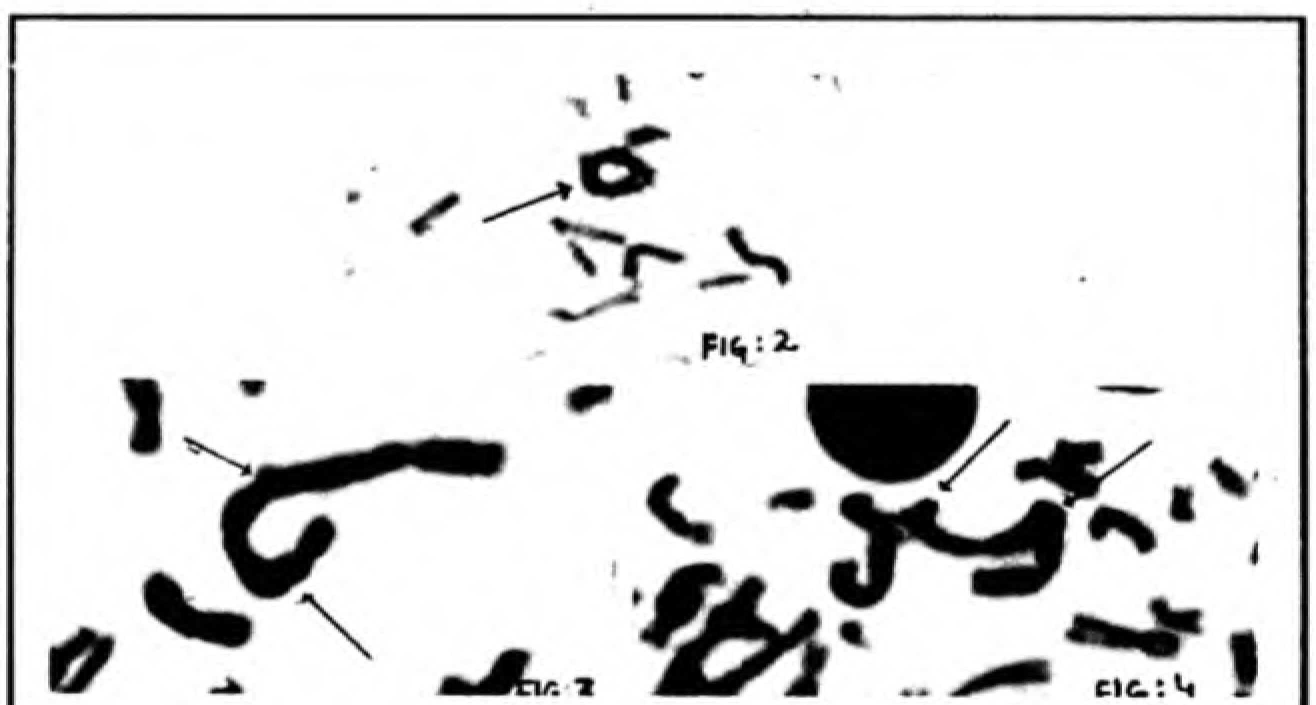
Ambiguous Genitalia has been recognised in man since antiquity. It is a condition where a child is born without any phenotypic sex. The role of chromosome study in these childeren has been convincingly advocated[1,2] Chromosome study helps in establishing the genetic sex of the child and through surgical intervention, genitalia is corrected accordingly.[3]

The present study was undertaken to find the chromosome patern in a child born with ambiguous genitalia. This study was found useful, in deciding about the future course of treatment.



Case Report:

A 2½ Yrs. old child was referred for correct assignment of sex through karyotypic evaluation. Mother had no history of drug ingestion or exposure to radiations in the antenatal period. Physical examination in the child showed ambiguous genitalia. Scrotum was bifid with a gonad in each half and the scrotal skin showed rugae on its surface (Fig. 1). The child had no other phenotypic anomaly. Histologically gonads were found to be the testis. Child showed intermittent abdominal distention and the generalized pallor since birth and died before attaining the age of three.



Chromosome analysis carried out from the short-term cultures of peripheral blood revealed sex-chromosome mosaicism (XO/XY). Some of the metaphase cells showed either a ring chromosome (Fig.2) or the telomeric associations among some of the chromosomes (Figs. 3&4). In these cells correct chromosome number could not be ascertained. Frequency of these cells was comparatively low.

Discussion:

Cytogenetic investigations in infants with Ambiguous genitalia are on record[1,3,4&5] and the present work is an addition to the existing data. The present case with respect to mosaicism is akin to the existing reports, however, it differs from the earlier reports with respect to the presence of a ring chromosome and telomeric associations seen among some of the chromosomes.

Reports on structural abnormalities such as deletions and ring chromosome formation in children with ambiguous genitalia exists in literature[2,3], but structural abnormality like telomeric associations among chromosomes in ambiguous genitalia have been reported for the first time.

Ambiguous genitalia in the patient under report is probably the result of mosaicism (XO/XY).

The presence of testes in the bifid scrotum might be

From the Department of Bio-Sciences Human Cytogentic Lab (Gupta) and Department of Surgery and Blood Transfusion (Goswami, Raina) Govt. Medical College, Jammu, India

Received June 1998 Accepted December 1998

Correspondence to : Dr. Subash Gupta, New Campus, University of Jammu, Jammu-Tawi - 180004

the result of XY cell-line, thus, supporting the concept of an interaction between autosomal genes and genes on Y-chromosome.[6]

The phenomenon of telomeric associations and stikiness of chromosomes in Thilerage-Welssenberg syndrome and in Ataxia telangectasla[7] has not so far been reported in cases with ambiguous genitalia. The presence of such abnormalities along with ring chromosome in the present case might be held responsible for recurrent abdominal distention and death of the child in infancy.

References:

1. Ayuso MC, Ramous MC, Bella A, Jimenez A, Sanchezcascos Herrara JL: Cytogentic and clinical findings in ten 45, X/46, XY patients. Clinical Genetics 1984; 25: 336-41.
2. Baramki TA. Treatment of congenital anomalles in Girls and Women. J Reprod Med 1984;6:376-84.
3. Dicholkar V and Mehta LN: Variant of Y-Chromosome VI. ALL Ind. Congr. Cyt. and Genet. Jammu (Abt) 1987; 161.
4. Rosenberg C; Frota-pessoa O; Vianna-Morgante AM; Chuth: The phenotypic spectrum of 45, X/46, XY individuals Am J Med Gent 1987; 3:553-59.
5. Shah VC; Krishnan-Murthy DS; Sabita-Roy; Contractor PM; Sha AV: True hermaphrodite 46, XX/46, XY, Clinical, cytogenetic and histopathological studies in J pediatr. 1982; 49: 885-90.
6. Eicher EM: In prospects of sexing mammalian sperm. Amann RP and Seldel Jr GF (eds), Colorado Association University Press, Boulder, Colorado 1982; 121-30.
7. Gandotra Arun; Sharma DB; Sasan AS; Gupta Subash: Two sibs with Ataxia telanglectasia PCNI, 1995 1-3, 46 (Abst.)

With Best Compliments From

SUPREME SYNDICATE

Complete Hospital and Laboratory Furnishers and
Pharmaceutical Distributors

267, NURSING GARH, SRINAGAR-190 001 (KASHMIR) PHONES : 471528, 478712; FAX : 0194-430645

AUTHORISED STOCKISTS FOR:

CHEMICALS:
- **E.Merck (I) Ltd.**
- **B.D.H. Chemicls**
- **S.D.Fine Chem. Ltd.**
- **Hi-Media Laboratories**

GLASS WARE:
- **Durani (German) Glass Ware**
- **Blue Star Glass Slides & Cover Slips**

EQUIPMENTS:
- **Getner Microscopes**
- **Suvira Audio Visual Equipments**
- **Sipcon Microtones/Tissue Processors**
- **Jindal Lab. Equipments**

Acrokeratoelastoidosis of Costa - An Atypical Presentation

Qazi Masood Ahmad, M.D.; Iffat Hassan, M.D.; S.Manzoor Ahmad, M.D.; Shugufta Parveen, M.B.B.S.

***Abstract:** An atypical case of acrokeratoelastoidosis occuring in a seventeen year old female right from birth is being reported in view of its unique presentation.*

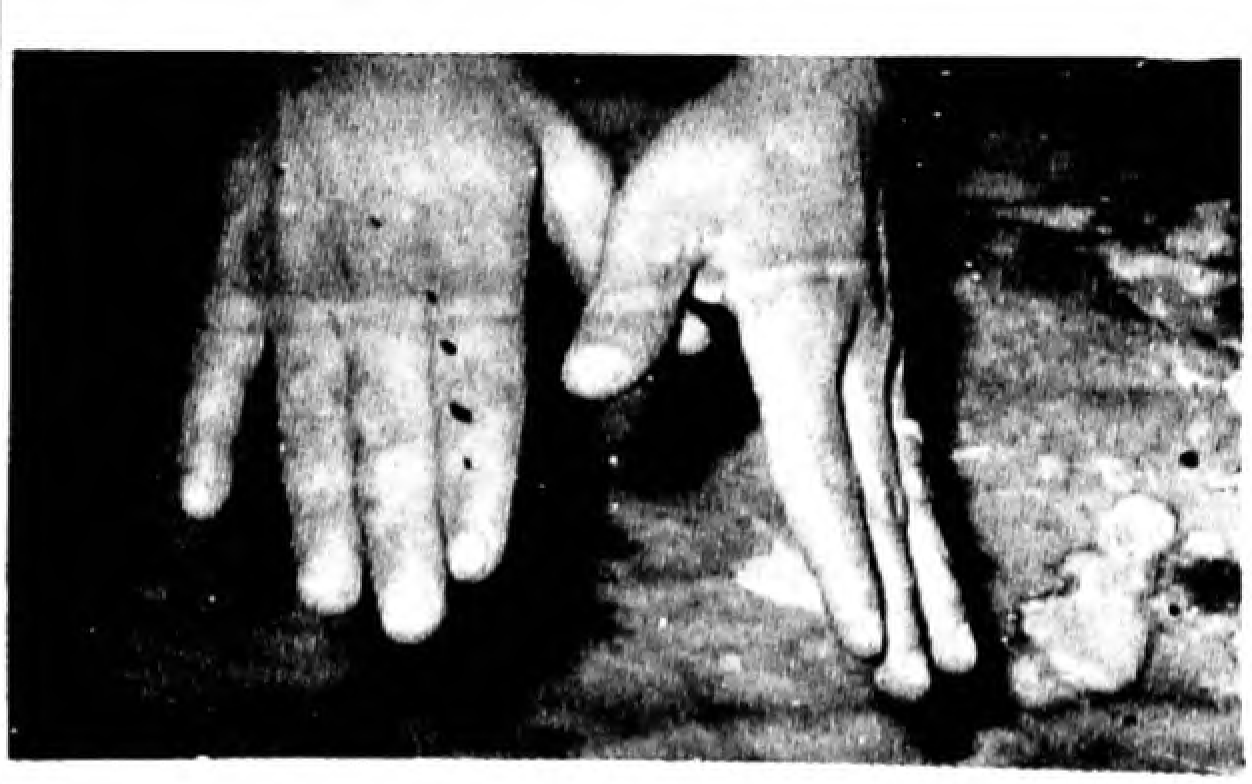
***Key words:** Acrokeratoelastoidosis*

JK-Practitioner 1999; 6(1): 68-69

Case Report

A seventeen year old female, product of a non-consanguinuous marriage presented to us with a history of multiple papules over the hands since birth. Apart from a cosmetic disfigurement, the lesions were asymptomatic. There was no history of excessive sweating or family history of similar lesions.

Her general physical and systemic examination was within normal limits. Cutaneous examination revealed multiple hyperkeratotic and transluscent papules at the junction between the palmar and dorsal skin especially along the contiguous borders of the thumbs to the tip of index finger (Fig.1). The papules were confluent at places. Few papules with confluence were also present on the palmar as well as the dorsal aspect of both hands. Feet were spared. There was no evidence of any actinic damage. Examination of the hair, teeth and nails did not reveal any abnormality. Skin biopsy from one of the papules revealed hyperkeratosis of the epidermis along with fragmentation of elastic fibres in the dermis.



(Fig. I)

Discussion

Since the initial description of acrokeratoelastoidosis by Costa in 1952, cases which were clinically and histologically similar have been reported by several authors[1-3].

The disease process usually begins in childhood or adolescence and the age of onset varies from 3 to 47 years. Most cases present during the second and third decade. Lesions start as firm pearly papules usually localized to hands and/or feet, but occasionally affecting the lower legs also. On the hands and feet, the most characteristic site of occurrence is the line of trangredience i.e., the boundary between the dorsal and palmar (or plantar) skin notably in the space between the thumb and fore finger and also irregularly along the line of palmodorsal junction on the thenar eminence.

The histological hallmarks of acrokeratoelastoidosis are epidermal hypertrophy with acanthosis and marked hyperkeratosis and coarse fragmentation of elastic fibres in the reticular dermis which is more marked in the deeper layers.

Sporadic occurrence has been postulated for most cases of acrokeratoelastoidosis. However, Costa reported ten cases in one family and three in another and there were twenty one members affected in three generations of a family reported by Jung et al in 1974 for which autosomal dominent mode of inheritance was suggested[1,3]. The incidence of this disorder seems to be unaffected by sex and race and the exact cause is unknown.

Highet et al[4] described two clinical syndromes of acrokeratoelastoidosis with the histological features originally described by Costa.

I. An idiopathic, sometimes familial form without associated actinic damage with onset usually in youth.
II. Lesions developing later in patients with existing actinic damage, and in whom repeated trauma may

From the Department of Dermatology, STD & Leprosy, GMC, Srinagar, India (Qazi, Hassan, Ahmad, Parveen)

Received March 1998 Accepted September 1998

Correspondence to : Dr. Qazi Masood Ahmad, Head Department of Dermatology, Govt. Medical College, Srinagar

also be important.

A third type of presentation with clinical features of acrokeratoelastoidosis but histologically distinct has also been proposed.

Other close variants of acrokeratoelastoidosis include focal acral keratosis[5], keratosis punctata of the palmar creases[6], degnerative collagenous plaques and porokeratosis of Mantoux. Acrokeratoelastoidosis linearis manus has also been reported by Malkit Singh et al[7] in a 52 year old person showing typical lesions of acrokeratoelastoidosis without any evidence of actinic damage or repeated trauma.

Our case differs in various ways from the classical cases described by Costa and other workers as the lesions were noticed right from birth, there was sparing of feet and there was no evidence of actinic damage or repeated trauma although the histopathological findings were same as those described by Costa.

Since there was no positive family history, our patient seems to have inherited this disorder in a sporadic fashion.

References:

1. Jung EG, Beil FV, Anton-Lamprecht I, Greten H, Nemetschek T. Acrokeratoelastoidosis Hautarzt. 1974; 25: 127-33.
2. Poiares Baptista A. Acrokeratoelastoidosis. Trabalhos da Sociedale portuguesa de Dermatological Venerelogia 1963; 21: 163.
3. Costa OG. Acrokeratoelastoidosis. Arch Dermatol 1954; 70: 228-31.
4. Highest AS, Rook A, Anderson JR. Acrokeratoelastoidosis. Br J Dermatol 1982; 106:337-44.
5. Dowd PM, Harman RM, Black MM. Focal acral hyperkeratosis. Br J Dermatol 1983; 109: 97-103.
6. Weiss RM, Rasmussen JE. Dermatosis punctata of the palmar creases. Arch Dermatol 1980;116:669-71.
7. Singh M, Kanwar AJ, Bharija SC, Mahdi I, Mangoush M, Belhaj MS. Acrokeratoelastoidosis Linearis Manus. Indian J Dermatol Venereol Leprol 1987; 58:298-99.

With Best Compliments From

KASHMIR PHYSIOTHERAPHY
&
REHABILITATION CENTRE

HRDC CAMPUS, POST OFFICE LANE, RAJBAGH, SRINAGAR-8
TELE : 450920

Cleft-Hand with Deafmutism

Rauoof M.A., MB; Wani M.A., MD, DM; Kadla S.A., MD; Malik J.A., MD

***Abstract:** Cleft-hand is a rare congenital deformity in which one or more of the central rays of hand are variably deficient or absent with a characteristic cleft in the metacarpus. Other congenital anomalies may co-exist. We report the incidental finding of a peculiar type of this deformity in an adult who presented with Pott's Spine.*

***Keywords:** Cleft-hand, Lobster-Claw Deformity, Deafmutism, Non-familial.*

JK-Practitioner 1999, 6(1): 70-71

Case Report

Ms. BK a normally menstruating 40 year old unmarried female got admitted with spastic paraplegia of 1½ month duratioon. The clinical diagnosis of Pott's spine was substantiated by radiological and laboratory data. The patient was put on antitubercular treatment and referred for surgical intervention. Routine physical examination revealed a deafmute female with scars of small-pox on face. There was a V-shaped central cleft in the right hand with absent middle finger. Both the feet showed central defects as well. The deformities were present from birth and there were no such deformities for four known generations from the index case. The patient's lips, palate, ophthalmological examination and urethral meatus were normal and bladder catheterization non-problematic. Cardiac examination, electrocardiogram and chest X-ray were unremarkable and IV pyelogram was normal. The limb roentgenogram findings are summarized below (Table 1, Figs. 1&2)

(Fig. I)

TABLE -1

Extremity	Clinical	Carpus	Metacarpus/	Phalanges	Remarks
Left hand	Normal	Normal	Normal	Normal	Normal
Right hand	Absent middle	Normal	Hypoplastic *MC3	Absent central ray	Typical cleft hand
Left foot	Absent 2nd & 3rd toes	Normal	Absent *MT2 Hypoplastic MT3	Absent 2nd & & 3rd rays	3-toed cleft foot
Right foot	2 toes only (1st & 5th	Normal	Absent MT2 Hypoplastic MT3	Absent 2nd, 3rd & 4th digits	Bidactylous cleft foot
			MT4 and MT5 together supporting a single proximal phalanx which in turn ->2 middle plalanges -> 2 distal phalanges in a single soft tissue structure or digit (? Syndactyly 4 & 5)		

*MC = Metacarpal (3 = 3rd from the radial side)

MT = Metatarsal

Discussion

The terms cleft-hand, lobster-claw hand, central hypoplasia, oligodactyly and ectrodactyly are all used interchangeably, albeit inappropriately, to refer to a spectrum of congenital central deficiencies ranging from just the absence of a digit to the complete absence of a hand or foot[1]. Hartsinck (1770) published the first account of the true cleft-hand in a Touvingas or two-fingered Negro in Dutch Guiana[2]. Kummel (1895) coined the term 'cleft-hand'[3].

Cleft-hand is a rare anomaly reported as 0.4 (Rogala et al)[4] to 0.14 (Birch-Jensen)[3] per 10,000 live births accounting for only 2.3% of the total number of hand anomalies[5]. Sixty percent of the cases occur in males[6]. Many combinations have been described with absence of the central ray or rays and partial or complete preservation of the border rays being the most common[7]. Syndactyly is considered an element of split hand by many[8]. Reduced interphalangeal joint motion and symphalangism are common[9]. A cross-transverse bone, carpal coalescence, radioulnar synostosis and complex abnormalities of metacarpals (e.g. one metacarpal splitting to support two digits and vice versa) may be present[10,11]. Roentgenograms reveal the details of osseous structure. Tendon, vessel and nerve involvement is variable and only identifiable at surgery[12].

Two types of central defects are commonly described (table-2)[9,13]. Type-I (or typical) defect is familial, dominantly (autosomal) inherited with variable expressivity[14]. Skipped generations and recessive inheritance are also known genetic prognosis for unaffected offsprings must be guarded[5,15] Other

From the Department of Medicine (Rauoof), **Neurology** (Wani) **SKIMS, Soura (India), SMHS Hospital Srinagar Kashmir India** (Kadla) **and PGI of Medical Education and Research Centre Chandigarh, India** (Malik)

Received April 1998 Accepted Nov. 1998

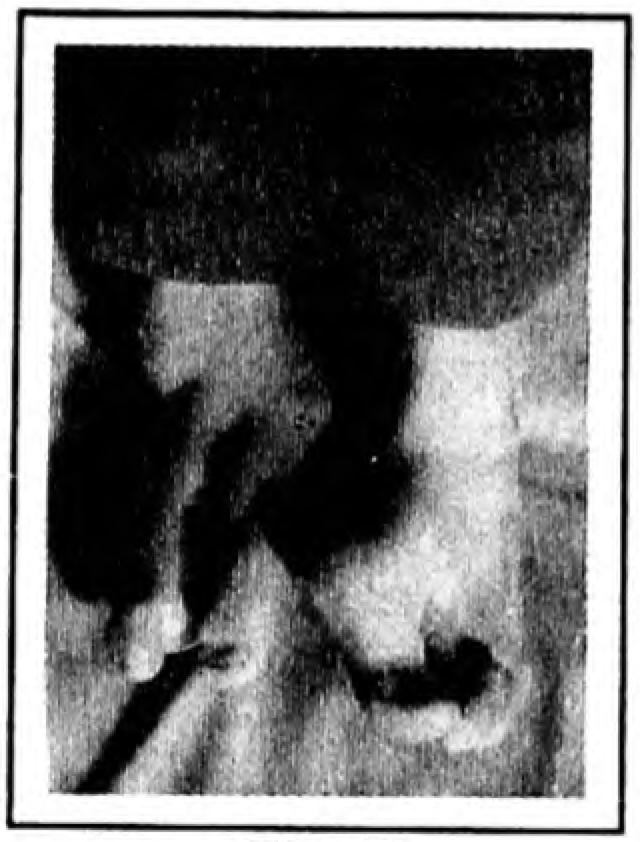
Correspondence to : Dr. Rauoof Malik, P.O. Box 843, GPO Srinagar - 190001, Kashmir

congenital anomalies are commonly associated e.g. cleft lip and palate, constricting band syndrome, radial or ulnar hypoplasia, genitourinary and cardiopulmonary abnormalities, deafness, cataracts, lens subluxation, etc.[8,16]. Adduction contracture of the first metacarpal is frequent[8]. Typical cleft-hand is viewed as a functional triumph and a social disaster[5].

TABLE -2: COMPARISON OF THE TYPES OF CLEFT HAND (9)

Feature	Type - I defect	Type - II defect
Laterally	Bilateral	Unilateral
Shape of defect	V-Shaped	U-Shaped
Foot Involvement	Present	Absent
Syndactyly	Common	Uncommon
Absence/deficiencies of finger rays	Middle ray absent (Sometimes index, rarely ring)	Several rays deficient
Associated anomalies	Common	Rare
Inheritance	Familial	Non-familial
Eponyms	Cleft-hand	Lobster claw hand, symbrachy-dactyly, ectrodactyly

The type-II (or 'atypical') central defect is nonfamilial and more handicapping; extreme cases may produce monodactylous or even adactylous hand. Thumb and little finger are often hypoplastic and "nubbins" of other digits may be present. The term "lobster-claw" is better applied to the fully developed atypical type of the defect[5]. In symbrachydactyly, finger stumps and rudimentary nails are present and severe forms involve the ulnar side of the hand. In contrast, bones may be absent or malpositioned in cleft-hand - never rudimentary; further radial side is predominantly involved[17]. Lately the term 'atypical cleft-hand' has been deleted in favour of symbrachydactyly by decision of the Vth Congress of the International Federation of Societies for Surgery of the Hand, Paris; 1992[18].


(Fig. II)

A type-III defect is described by some in which there is complete absence of 1, 2 or 3 central rays. No anomalies are associated and no inheritance pattern has been established[16]. The case described above had many peculiar features e.g. unilateral type-I defect in right hand, no family history, predominant involvement of feet.

The exact mechanism by which these defects are produced is not known. Maisles theory of centripetal suppression blames the progressive insult to the developing hand plate in or about the 7th week of gestation. Mildest cases may produce a simple cleft without any tissue deficiency; progressive suppression of radial rays eventually leads to the loss of ulnar rays - extreme forms leading to mono - or even adactyly[19]. This explanation is probably insufficient for type-II and type-III defects which have been alternatively explained by altered apoptosis occurring in the developing limb to form the normal webs between the digits with improperly programmed release of lysosomal enzymes during interdigital necrosis producing the cleft defects[16].

Because of the coincidental development of limb bud and genitourinary tract during embryogenesis, an intravenous pyelogram is indicated in any child born with thus deformity[20]. Improving function is the major consideration in the management of cleft hand while cosmesis is secondary. Early surgical correction between the ages of 6 and 24 months is recommended [8,9,15]. In feet, surgery may be required for cosmesis or to facilitate shoe wear.

References:

1. Poznanski AK. The hand in radiologic diagnosis. WB Saunders, Philadelphia, 1974; 183-87.
2. Hartsinck JJ. Beschryving Van Guiana, of de wilde kust in Zuid America Vol 2. Gerritt Tielenburgh, Amsterdam, 1770; 811-12.
3. Birch-Jensen A.Congenital deformities of the upper extremities. Ejnar Muntsgaads Forleg, Odense, Denmark, 1949; 46-76.
4. Rogala EJ, Wynne-Davis R, Littlejohn A, Gormley J. Congenital limb anomalies: Frequency and etiological factors. J Med Genet 1974; 11:221-33.
5. Flat AE. The care of the congenital hand anomalies (cleft-hand and central defects). CV Mosby, St. Louis, 1977; 265-85.
6. Watari S, Tsuge K. A classification of cleft-hands, based on clinical findings. Plast Reconstr Surg 1979; 64:381-89.
7. Daniel CR. The upper limb. In: Paediatric Orthopedics Vol. 2. Wood WL and Winter RB (Eds.). JB Lippincott Co, Philadelphia, 1978; 685-715.
8. Wood VE. The cleft hand (central deficiencies). In: Operative Hand Surgery 2nd edn. David P Green (Ed). Churchill Livingstone, 1988; 275-91.
9. Upton J. Congenital anomalies of the hand and forearm. In: Plastic Surgery McCarthy (ed). Vol.8 The Hand. Part 2, May and Littler (eds). WB Saunders Company 1990; 5213-5398.
10. Wood VE. Treatment of the triphalangeal thumb. Clin Orthop 1976; 120: 180-200.
11. Wood VE, Flatt AE. Congenital triangular bones in the hand. J. Hand Surg 1977; 2: 179-93.
12. Milford L. The split (cleft) hand. Presented at symposium on "Congenital Hand Deformities" sponsored by American Society for Surgery of the Hand, Atlanta may 1978, 4-6.
13. Barsky AJ. Cleft hand: Classification, incidence and treatment. J Bone Joint Surg (Am) 1964; 46: 1707-19.
14. David TJ. The differential diagnosis of the cleft hand and cleft foot malformations. Hand 1974; 6: 58-61.
15. Graham JB, Badgley CE. Split-hand with unusual complications. Am J Hu Genet 1856; 7: 44-50.
16. Peter RC. Reconstruction of the child's hand. Lea & Febiger, Philadelphia, 1991; 175-83.
17. Buck-Gramcko D. Handchirurgie. Band I, Allgemeines Wahloperationen. Thieme, Stuttgart, 1981.
18. Graham Lister. The Hand. Diagnosis and Indications. 3rd edn. Churchill Livingstone 1993; 468-73.
19. Maisles DO. Lobster-claw deformities of the hands and feet. Br Jr Plast Surg 1970; 23(3): 269-81.
20. Wood WL, Charles TP and Peter LM. The Foot In: Paediatric Orthopedics Vol.2 Wood WL and Winter RB (Eds.). JB Lippincott Co, Philadelphia, 1978; 911-97.

Chronic Traumatic Diaphragmatic Hernia in a Child -An Unusual Presentation

Ghulam Nabi Lone, M.Ch.; Rajendar Kumar Suri, F.A.M.S, F.I.A.C.S; Shyam K.Singh Thingnam, M.Ch.

***Abstract**: Traumatic diaphragmatic hernia continues to be a challenge to the surgeon. Delayed presentation is known but an uncommon entity. We report the case of an eight year old child with diaphragmatic hernia that manifested after three years of original trauma. Diagnosis was established on the basis of chest radiography and clinical signs. Surgical treatment cured the patient.*

***Key words**: Diaphragmatic hernia, Trauma, Radiography*

JK-Practitioner 1999; 6(1): 72-73

Introduction

Blunt trauma due to high speed motor vehicle accidents and high velocity missile injuries is the major cause of traumatic diaphragmatic hernia. This devastating outcome of diaphragmatic injury was reported by Ambroise Pare in 1579, when he discussed a French captain who initially survived a gun shot wound to the abdomen but died eight months later due to gangrene of herniated colon[1]. Traumatic diaphragmatic hernia remains a difficult problem to diagnose in children in particular[2]. Chronic hernia is an uncommon presentation. An early index of suspicion can be life saving in a victim of multiple injuries.

Case Report

An eight year old, school going male child was brought to our outpatient department with the symptoms of vomiting, abdominal cramps, occasional chest pain on left side, and mild breathlessness of recent onset. Medical records indicated that the child had sustained trauma while travelling in a bus 3 years before. Initially the child was treated at a local hospital for suspected abdominal trauma and his chest x—ray was normal and his abdominal ultrasound did not reveal any visceral injury. He was discharged after 24 hours of observation.

On physical examination, trachea was deviated to right side. Breath sounds were reduced on left side. Apical impulse was shifted to right parasternal region. Bowel sounds were audible on left side of chest.

Blood gas analysis showed pH of 7.38, PaO_2 of 82mHg, $PaCo_2$ of 43 mmHg. Chest x-ray showed diffuse haziness in left chest and cardiac silhouette was shifted to right side. Left dome of diaphragm was ill defined and elevated. Left lower lobe was collapsed. Barium study revealed intrathoracic stomach on left side (Fig.I).

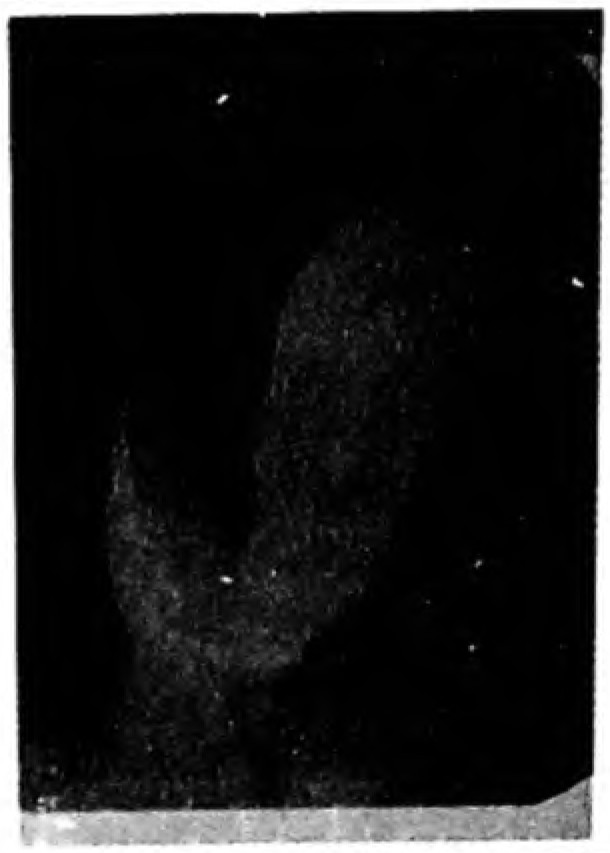


Fig.I: Revealing intra thoracic Gastric shadow on upper GI Barium Study

Exploration revealed collapsed left lower lobe and lingula. Dense adhesions were seen in left thoracic cavity and gastric herniation was seen through a small tear in left dome of diaphragm. The defect was repaired with polypropylene in two layers. There was no evidence of recurrence of hernia till last follow up.

Discussion

Traumatic diaphragmatic rupture is a rare childhood injury and is commonly misdiagnosed and ignored[2,3].

Traumatic diaphragmatic hernia was first described by Sennertus in 1541. It was not until 1853, that the diagnosis was first made by Bowditch in a living patient[2]. However, even today difficulty and delay are frequently encountered in making the diagnosis.

Traumatic diaphragmatic hernia appears to be a rare injury in childhood and infancy unlike the adults, as found in the literature also. Blunt trauma accounts for the majority of the cases in childhood. However, penetrating diaphragmatic injuries assume a more important role in adolescents and young adults.

The mechanism of diaphragmatic rupture in patients with blunt trauma is presumed to be due to abrupt and

From Post -graduate Institute of Medical Education and Research Chandigarh, India (Lone, Suri, Thingnam)

Received March 1998 Accepted September 1998

Correspondence to : Dr. G.N.Lone, Deptt. of Cardio-thoracic & Vascular Surgery, SK Institute of Medical Sciences Soura, Srinagar, Kashmir (India) 190011, Post bag No. 24. Tel No. (O) 0194-422592 Ext. 460; (R) 0194-422592 Ext. 398

inordinate increase in intrabadominal pressure from a forceful insult to the upper abdomen or a crush injury to the abdomen[4,5]. This results in a linear tear near the apex of the hemidiaphragm through the central tendon[6]. The diaphragm also gets injured in the setting of blunt thoracic trauma, in which diaphragm is torn by a fractured rib or avulsed at its origin on the chestwall[7]. Whatever the mechanism, the magnitude of the trauma is great, accounting for the frequent association with other injuries.

The majority of blunt traumatic diaphragmatic hernias follow the rupture of the left hemidiaphragm. This appears to be due to relative weakness of the left hemidiaphragm versus the right[7], or that the right dome is protected by the liver[6,7]. Recent data, however, suggests that the two are equally susceptible to rupture but the right sided injuries are more likely to be associated with rapidly fatal injuries in the form of major hepatic parenchymal or retrohepatic caval injuries and result in higher field mortality[8].

In the absence of associated abdominal or thoracic injuries, diaphragmatic perforation can remain unrecognised until actual herniation of intra-abdominal organs results. The herniation results in abdominal symptoms from strangulated gut or respiratory compromise. Herniation is thought to occur because of pressure gradient across the diaphragm, intrathoracic pressure being negative in relation to the intra-abdominal pressure[2].

Herniation may be *acute*, which is seen at the time of injury, *delayed* which is seen after an interval of time since the original injury and *chronic*, manifested by recurrent mild symptoms until visceral incarceration or respiratory symptoms bring the patient to the attention of a doctor[6]. Delayed hernia has been reported as late as 45 years after original trauma[1,9]. However, our patient presented 3 years after the trauma which according to the father of child was trivial. His earlier medical records had shown minimal haemmorhagic pleural effusion, mild elevation of the left dome of diaphragm. He remained asymptomatic for 3 years. But recently, he had several bouts of bilious vomiting and abdominal cramps.

The diagnosis of diaphragmatic hernia can be difficult. However, the vigil and suspicion of diaphragmatic tear by the clinician can prevent the herniation to a large extent while attending to a trauma victim. The initial x-ray film rarely detects diaphragmatic tear, though often abnormal. X-ray may indicate a picture of small pleural effusion with atelectasis or elevation of hemidiaphragm[2]. Abdominal CT scanning can detect the possibility and severity of visceral injury and can rule out herniation but rarely allows identification of the isolated diaphragmatic tear - the site for the future herniation[2].

Barium study of upper and lower gastrointestinal tract remains the single tool for the confirmation of herniation. On initial exploration for suspected intra-abdominal injuries, emphasis should be laid on excluding the diaphramatic fear. However, isolated diaphragmatic tear poses a significant risk of delayed herniatioin[4], as in the case of our patient.

Stomach, spleen, colon, liver, small intestine, omentum are the commonly hernial contents[1]. The treatment of traumatic diaphragmatic hernia is exclusively surgical and should be performed shortly after the diagnosis is made.

Acute hernias are preferrably repaired by abdominal approach because it allows the repair of the associated abdominal visceral injuries. However, 50% of right sided hernias require thoracotomy to correct the defect due to inaccessibility[1].

Delayed and chronic diaphragmatic hernias are repaired by thoracotomy[1,9]. It is much easier to reduce the herniated contents after adhesolysis in thoracic cavity, in contrast with abdominal approach. The diaphragmatic tear is repaired by double layer of non-absorbable sutures. However, large defects need a prosthetic material.

We repaired the defect by polypropylene in double layer after reducing the stomach and till late follow up, there is no evidence of recurrence of hernia.

References:

1. Gregory L, Brown and J. David Richardson: Traumatic diaphragmatic hemai: A continuing challenge. Annals of Thor Surg, 1985; 39:2.
2. Juan E Sola, Peter Mattei, Walter Pegoli et al: Rupture of the right diaphragm following blunt trauma in an infant: Case report. J Trauma, 1994; 36:3.
3. Myers NA: Traumatic rupture of diaphragm in children. Aust NZ Surg 1964; 34:123.
4. Radhakrishna C, Dickinson SJ, Shaw A. Acute diaphragmatic hernia from blunt trauma in children. J Pediatr Surg, 1969; 4:5.
5. McCune RP, Roda CP, Eckert C: Rupture oof diaphragm caused by blunt trauma. J Trauma, 1976; 16:7.
6. Desforges G, Strieder JW, Lynch JP et al: Traumatic rupture of diaphragm. J. Thoracic Surg, 1957; 34:779.
7. DeOliveira F, Oliveira FJ, Oneirs A: Traumatic diaphragmatic hernias: A report of 19 cases. Can J Surg, 1982; 26:6.
8. Maull KI: Diaphragmatic rupture. In Cameron JL (ed): Current Surgical Therapy, Vol. 4, St. Louis, Mosby-yearbook, 1992; pp 840-844.
9. Childress ME, Grimes OF: Immediate and remote sequelae in traumatic diaphragmatic hernia. Surg Gynecol Obstet, 1961; 113:573.

"Sweat Glands in Man and Horse"

Abdul Ahad M.S.; Shameem Jabeen M.D.; Mehmood Ahmad Mughal M.D.

Abstract: *Light microscopic study of the sweat glands of man and horse was undertaken under the same histological conditions. Two types of the secretory cells were seen in the secretory portion of the sweat glands of both the species. In addition, the human sweat glands showed one more incomplete layer of cells between these two types of cells and the outer layer of myoepithelial cells. These could be resting/stem cells for the other two types of cells. In man the mode of secretion is epicrine whereas in horse both eccrine as well as aprocrine mode of secretion was noticed.*

Key Words: *Myoepithelial cells, Eccrine (Epicrine), Apocrine, Intraepidermal, Intradermal, Acinus.*

JK-Practitioner 1999; 6(1): 74-77

Material and Methods:

Skin pieces from the abdomen limbs and neck of six horses (Equs Caballus) were obtained either during debridement of wounds or excision of cysts at these sites or after euthanasia for various reasons. None, however, had any skin disease at the site of collection of the skin piece. Six pieces of the skin from the same sited in four male and the three female adult human beings were collected during operations for the thyroid, dermoid cyst-excision and abdominal surgeries. 2-3 mm thick skin pieces were immediately put in formal saline 10%, dehydrated in ascending grades of alcohol, cleared in xyline, and the wax block were prepared. 5-7 um (Micrometer) thick sections were prepared and stained with hematoxylin and eosin, Masson's trichrome, Van Gieson's, Gordon and Sweets' and Orcein methods.

Introduction:

Horse and the man have been enjoying close association since times immemorial. Both sweat under various conditions besides insensible perspiration. In human beings there are 2.5 million sweat glands covering an area of 90cm^2 if the glands are consolidated to form one localised gland[1,2]. These glands are present on palms, soles, face and the rest of the body except a few sites. During severe heat and higher humidity a man can sweat out 4 litres per hour for short periods[2]. Ordinarily a body loses 600ml of water per day through the lungs and skin by evaporations[1,2]. In cystic fibrosis there is elevated sodium level in the sweat[2]. In uraemia, when the kidneys are unable to get rid of the body urea, concentration of urea in the sweat is increased[3]. After evaporation crystals of urea may be seen, especially on the lips-Urea-frost. Sweat glands are activated by cholinergic sympathetic nerve fibres and a few adrenergic nerve fibres in man whereas in horse their action depends upon hormonal stimulation[4]. The human sweat glands possess 30 times more carcinoembryonic antigen than the serum[5]. The human sweat glands have been held to possess a constituent which is attractive to mosquitoes[6]. This was supported by Brown[7] who held alanine and lysine attractive to Aedes-aegypti. Skinner[8] confirmed this concept.

The sweat glands are of two types-apocrine and eccrine. The structure and the mode of secretion differs between the two types. Absence of the sweat glands without any other ectodermal defect has been observed[9]. The glands have two parts—the acinar part and the duct. The duct has two parts—the intra-dermal and the intra-epidermal part. In human beings the apocrine glands are restricted to the axillae, groin and areda of nipple. The aim of the present study is to find the light microscopic differences between the sweat glands of the two species that are present over the body excluding the axillae, groin areola and areas near various body apertures.

Observations:

In horse skin numerous sweat glands were observed which were almost exclusively situated in the superficial zone of dermis amidist sebaceous glands. These were large with wide lumen. Many arterioles and capillaries were seen in the vicinity of the glands situated in the loose tissue. The acini were immediately surrounded by loose connective tissue consisting of colleagen and elastic network within which numerous fibroblasts were seen. Each acinus had cells in two layers—the inner layer of

From Department of Anatomy, (Ahad) Physiology (Jabeen) Govt. Medical College Srinagar, Kashmir India and the department of Physiology, (Prof. Mughal) Al-Fateh University of Medicine, Tripoli (SPLAJ)

Received August 1998 Accepted November 1998

Correspondence to : Dr. Abdul Ahad M.S. Professor Histology, Al-Fateh University of Medicine, Tripoli (SPLAJ).

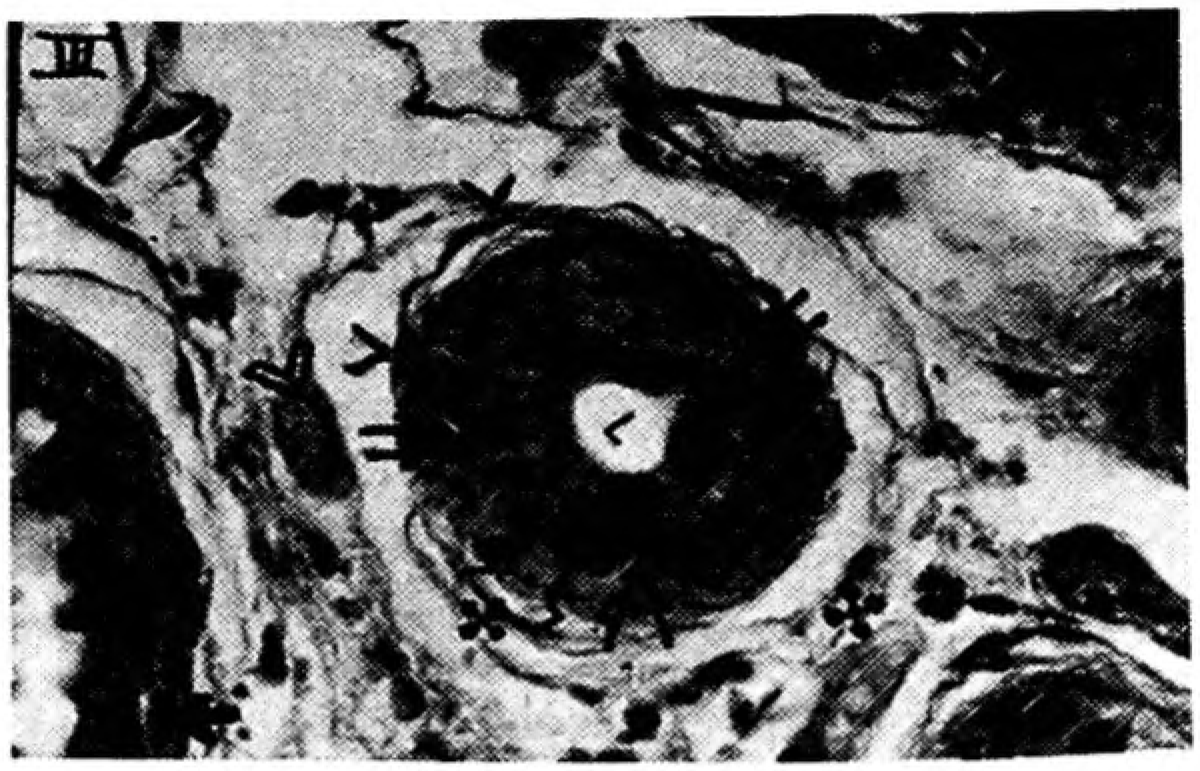


Fig. I: Photomicrograph (Mag 15x40)
Human Sweat Glands showing clear cells (Double arrows), Daru cells (Zigzag arrows), Middle layer cells (M), Myoepithelial cells (arrowheads), Lumen (L), Thick basement membrane with myoepithelial cells in it (Thick arrow), Arteriole (Hollaw arrowhead), connective tissue (asterisk)

the acinar secretory cells and an outer layer of myoepithelial cells. The acinar proper cells vary in shape from cuboidal to columnar. These rest on a thick basement membrane. The nuclei are round and central. The cytoplasm exhibited a reticulated appearance especially in the supranuclear part. Some cells with clear cytoplasm were seen. A few cells with thick luminal border were there. Intercellular walls were not well defined. A few cells with lost apical portion of the cells were visible. These dark and clear cells were seen in the ratio of 18:1 on an average in any section of the acinus examined. Some cells were seen with the projecting luminal wall as if ready to burst. Vaneieson's stain exhibited brownish-pink reticulated material especially adjoining the cells with the lost apical cytoplasm or projecting luminal wall.

Brownish yellow material filled the lumen of a few acini that had low epithelium. This material stained pink by hematoxylin and eosin stain.

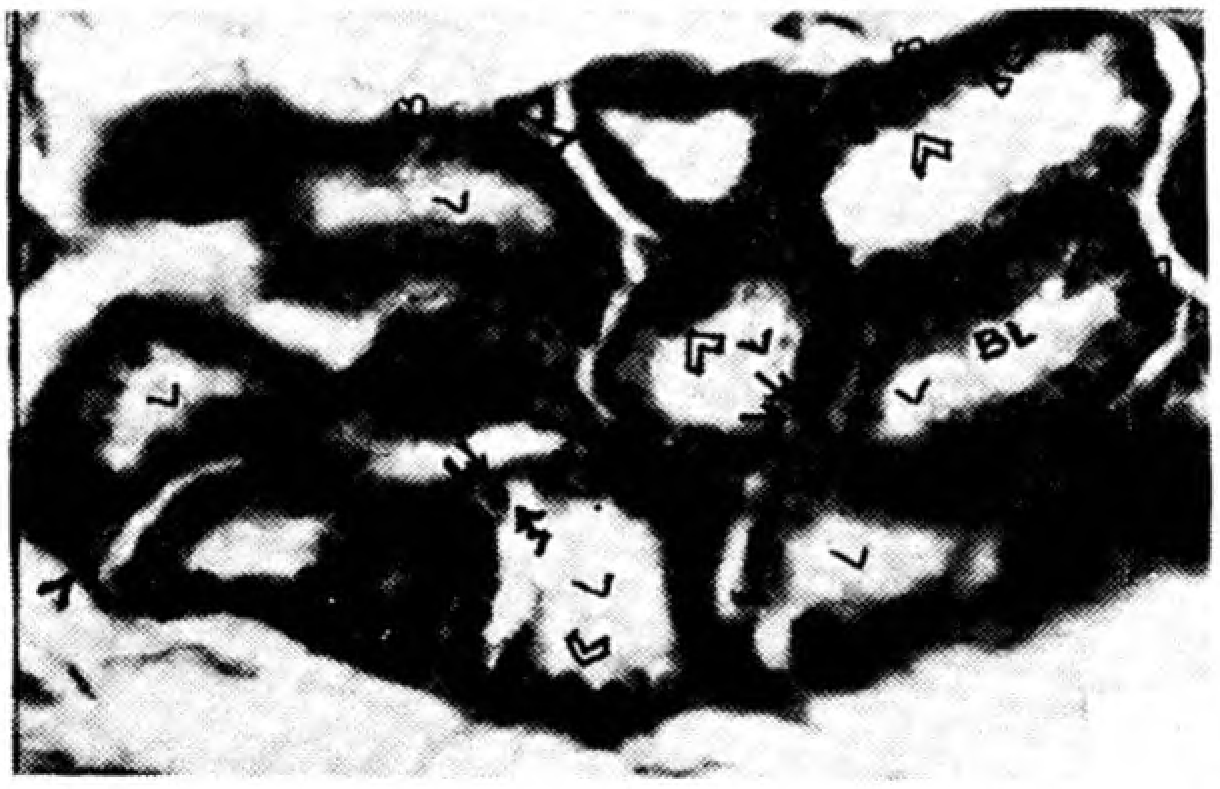


Fig. II: Photomicrograph (Mag 10x40)
Harse Sweat glands showing clear cells (double arrows), Dark cells (Hollow arrow heads), Ruptured cells (Zigzag arrow), Myoepithilial cells (arrow heads), Lumen with secretion inside (L), Cells with bulging Luminal surface (BL) and thick basement membrane (B)

The outer layer of cells consisted of elongated cells with mostly long spindle shaped nuclei. The long axis of these nuclei was at right angles to the long axis of the acinus proper cells forming the inner layer. Depending upon the plane of section some nuclei were seen to be rounded, ovoid or dot shaped. These cells were situated in the deepest part of the basement membrane.

Epidermis is very thick in horse and, hence, the intra-epidermal portion of the sweatgland ducts equals that of intradermal segment in length. The ducts were lined by stratified cuboidal epithelium. The nuclei were more darkly stained than the nuclei of the acinar cells. The lumen of the intraepidermal portion of the duct was slit like and lined by one layer of flattened cells with long axis parallel to that of the long axis of the duct. The duct cells were surrounded by longitudinally disposed collagen fibres. No myoepithelial cells surrounded the duct.

In human skin the sweat glands were seen almost exclusively in the deeper part of the dermis and superficial part of the subcutaneous tissue. Their number was far less than those in horse. The acini were surrounded by thinner bundles of collegen and a few elastic fibres. The acinar part of the gland had 2—3 layers of cells in the wall. The outer most layer of cells consisted of flattened cells with thinner and elongated nuclei. These myoepithelial cells were resting against the cells of the deeper layer but at some places in the superficial zone of the basement membrane instead of being very close to the secretory cells.

With hematoxylin and eosin staining all the cells gave the same appearance. VanGieson's stain differentiated two types of cells. Most of the cells had yellow coloured cytoplasm with brownish granularity. These flattened to cuboidal cells had oval to rounded centrally placed nuclei. The cells are smaller than in horse but crowded together for the same thickness of the section. A second type of cells with clear unstained cytoplasm on one side or all round the nucleus were seen. These cuboidal cells had rounded and centrally placed nuclei. Most of these cells had lesser area of their luminal surface exposed towards the lumen due to overlapping of the adjoining granular cells. The average ratio of the dark and clear cells examined in any section of the acini was 13:1. Some acini were seen to have one more type of the cells between the secretory and the myoepithelial cells. These were cuboidal or pyramidal cells with large centrally placed nuclei. The acini were widely separated from each other by loose areolar tissue than in horse.

The duct had two parts as in the horse. Human epidermis being thinner, the intraepidermal part of the duct was, therefore, shorter. The cellular details were the same as in horse except that very thin collagen fibres surrounded these ducts that were coiled. The lumen, too, was very narrow.

We have observed that the Myoepithelial cells are far less in number in horse than in man.

Discussion:

Sweat glands are important for water metabolism and temperature regulation of the body. Composition of the sweat is directly related with many metabolic processes in the body. Fall in the excretion of trace elements like iron in the sweat in anaemia is well known. Lot of sodium chloride, phosphorus and lactic acid is present in it. In horse the sweat is highly alkaline whereas its lactic acid content is 4 times than in blood in human beings[10].

Sweat glands are present in the superficial zone of dermis whereas in human ,beings these are in the deeper zone and in the subcutaneous tissue. This connotes that the sweat has to traverse a longer distance after its formation to come to body surface in human beings. The ducts have the longer intradermal part which will have better effect of changing the composition of sweat like aldosterone effect on these ducts. Aldosterone has the same effect on the sweat ducts as in the kidney tubules. In horse the epidermis is thicker and, hence, the intraectodermal part of the duct is longer. Ectoderm is avascular and, therefore, the functional efficacy of this intraepidermal portion will be totally different. Even otherwise the intradermal parts of the ducts in horse are shorter as the glands are very superficial. There are numerous arterioles and capillaries in the superficial dermis in horse which could have direct effect on the functional capacity of the acinar portion and the initial portion of their ducts. Horse does withstand extreme cold and the brunt of galloping overloaded during hot climate too. Mechanism of regulation of temperature has to be different and efficient for its survival.

The basal lamina (Basement membrane) is very thick in both the species which is in conformity with the findings of Kostowiecki et al[11]. In the secretory epithelium of both the species both the granular and clear cells are seen. Hematoxylin and eosin staining did not show these two types of cells. It is as observed by Munger and Brucilow[12]. VanGieson's stain which stains the cytoplasm yellow[13], could show two types of cells on the basis of staining of cytoplasm. This confirms the findings of Munger and Brucilow[12]. Functionally the clear cells are concerned with the active transport of ions and/or water[12] and the dark cells with protein secretion[14]. Transport of the proteins, water and ions could be expected to occur both in man and horse sweat glands. The present study does not conform to that of Munger's observation of finding of only one type of cell in the rat planter skin. Kurosomi and Kurosomi[15] held the darkness of the dark cells to be due to shrinkage which we could not confirm as the same results were observed in all the specimens and cell shrinkage could not be seen while staining by different stains even. We feel that the earlier presumption of this cell shrinkage does not hold true.

Excessive loss of protein in the horse sweat has been observed by Mevans et al[16] which could be explained by our finding of high ratio of dark cells in horse sweat glands.

The secretory cells in horse sweat glands are cuboidal or columnar whereas in human sweat glands these very in shape from squamous to cuboidal and columnar. This means higher activity in the horse sweat glands. The luminal surface of some horse sweat glands is projecting into the lumen or lost which connotes holocrine mode of secretion. The special features of the holocrine sweat glands is the presence of only one type of cells[17,18,19]. But, we have found two types of the cells in our present study in the horse sweat glands, which goes in favour of both the eccrine as well as holocrine mode of secretion in these glands. Ellis[18] believes that there are two types of sweat glands in human skin—the eccrine present all over the body especially over the palms and soles and apocrine glands present in axillae, areola of nipples, labia majora and circumanal regions whereas others[14] believe that all the cells of the sweast glands in human skin are merocrine. Some investigators correlate the function of the clear cells with holocrine mode of secretion[20]. Some postulate that the ducts of the sweat glands of apocrine type undergo metaplasia towards the sebaceous glands. This investigator[21] holds, again, vast differences in the duct of the apocrine and eccrine glands. We could not find these differences.

The presence of cells between the myoepithelial and the secretory cells in man could be resting cells which may replace secretory cells if and when need. It is in conformity with the postulation of Rupec[20].

Myoepithelial cells are far less in horse sweat glands than in human skin. Acetyl choline act on these cells in human sweat glands as the post ganglionic sympathetic secretion. This also connotes the well established mental and reflex sweating under the conditions of stress, internal and external temperature, vomiting or sweating on the head after taking chillies which stimulate reflex sweating by tastebud stimulation. This could be accurately mediated by the effect on the small blood vessel smooth muscle and abundant myoepithelial cells[2]. Similar complex may not be operating in horse and, therefore, the contractile elements is the myoepitheldial cells are lesser in number and smaller in size. This is in consonance with the findings of Uno[4] who holds horse sweating to be mediated through humoral effect. Selkut[2] mentions minimum nerve fibres supplying the equine sweat glands which could be further investigated.

Acknowledgment:

We are quite thankful to Dr. A.S.Najar B.V.Sc. and A.H. for his ready help in collection of equine skin specimens. The pieces of skin had to be collected from fresh skin wound sites or after euthanasia for various reasons. Similar skin pieces from the same sites i.e. abdomen, limbs or neck and head were provided by our friends in the Departments of Surgery and Gynae and obstetrics who had got these healthy skin pieces during routine abdominal or thyroid surgeries or repair of wound we thank them very much.

References:

1. Bijlani, R.L. Understanding Medical Physiology. 1995; 557-558. Jaypee Brothers Medical Publishers Ltd. New Delhi.
2. Selkurt, E E. Physioology, Ed. 5, 1984: 557-58 Published by Little Brown and company.
3. Ross, M H, Lyn, J. Romrell, Gordon, I K. Histology. A text and Atlas Ed II. 19: 384-387. Pub. Williams and Wilkin, 428 East Preston Street, Basltimoore, Maryland, USA.
4. Uno, H. Sympathetic innervation of the sweat glands and piloarrector muscles of macaques and human beings. J. Invest. Derm. 1971; 69/1: 112-120.
5. Penneys, N S, Nadji, M, Mc Kinneu, E C. Carcinoembrayonic antigen present in human eccrine sweat glands. J. Am. Acad. Dermatol. 1981; 414: 401-403.
6. Howlett, F.M. Parasitol. 1910; 2: 479 (Quated by Skinner W.A. et al.).
7. Brown, A W A. Bull of Entomol Res. 1964; 54: 675 (Quated by Skinner W A et al.
8. Skinner, W A, Tong, H, Pearson, T, Strauss, W. Maibach, H. Human sweat component attractive to mosquitoes. Nature. 1965; 207: 661-62.
9. Juhlin, L. Absence of Eccrine sweat glands without other ecotodermal defect. Acta. Derm. Venereol. Stockl. 1980; 60(1): 73.
10. Bankus, WJJ. Histology and Comparative Anatomy. A Text Atlas. (1974); 150-155. Published by Williams and Walkins Company, Baltimore.
11. Kostoowiecki, M, Ilewicka, K L. Affinity fo the basement membrane of the eccrine sweat glands for Weigert's elastic stain. P-Z. Mirosk. Anat. Forsch. 1971; 84/4: 520-534.
12. Munger B L, Brucilow, S W. The histopathology of the rat planter sweat glands. 1970; Anat. Rec. 169: 1-22. 1970; 169: 1-22.
13. Drupy R A B, Walington, E A. Carlton's Histological Techniques 1980; 5: 183. Oxford University Press, New York, Toronto.
14. Weater, P R, Burckitt, H G, Daniels, V G. Histology. A Text and Coloured atlas. Reprint 1981; 120-126. Pub. Churchill Livingstone, Edinburgh, London and N.Y.
15. Kurosomi, K, Kurosomi, U. Electron microscopy of the mouce eccrine sweat glands. Arch. Hist. Jap. 31/3:4, 445-475.
16. Mc Evan, Jenkinson, D, Montgomery, I and Elder. H Y. The ultra-structure of the sweat glands of ox, sheep and goat during sweating and recovering. 1979; J. Anat: 129/1: 117-140.
17. Beimpica, L, Monte, L.F. Secretory Epithelium of large axillary sweat glands; A cytochemical and electron Microscopic study. Am. J. Anat. 1965; 117: 47-72.
18. Ellis, R.A. Eccrine, Sebaceous and Sweat glands; In Ultrastructure of Normal and Abnormal Skin. 1967 a Ed. Lea and Febriger, Philadelphia.
19. Munger, B L. The cytology of the apocrine glands of cat and monkey a Z. Zeltforcsh 1965; 67: 373-383.
20. Rupec, M. The ultrastructure and acid phospatase activity in the sweat.glands with clear retixculated cytoplasm. Arch. Derm. Res. 1977; 258/2: 193-201.
21. Kurosomi, K. Fine structure of the human sweat ducts of eccrine and apocrine type. Arch. Hist. Jap. (Nigata). 1977; 40/3: 203-224.

Prognostication of Acute Renal Failure in Patients with Cholera

Pavel D. Kiritchenko

The renal failure in cholera has been described as a consequence of hypovolemic shock which induces acute tubular necrosis[1]. If the fluid deficit is not corrected it may lead to anuria, uremia, and death. Although adequate rehydration therapy in time is accessible in the early stages of cholera the problem of acute renal failure remains actual Azotorrhea may prolong diarrhea for cholera. More over, even successfully treated acute renal failure leads to chronic pyelonephritis in 44.8% of patients and to chronic renal insufficiently in 18.4%.

Materials and methods

The study included 54 patients with severe cholera which have been treated in Nicolaev hospital in 1995 (Ukraine). The diagnosis of cholera in all cases was confirmed by the identification of Vibrio cholerae El Tor, Ogava in the stool. The cases was considered severe if the patients weight loss exceeded 7%. The intravenous rehydration therapy was carried out by isotonic fluids: Dhaka Solution or (Quartasol). The latter included 4.75 g of NaCl, 1.5g of KCl, 2.6 g of sodium acetis and 1.0 g of sodium bicarbonate at in 1 litre of apyrogenic water. Oral rehydration was carried out by (rehydron) containing 3.5 g of NaCl, 2.5g of KCl, 2.5g of sodium citratis and 10.0 g of glucose at 1 litter of water.

The estimation of renal function was perfomred by clinical data and definition of the serum creatinine concentration. The main clinical sign indicating acute renal failure in all patients was oliguria or anuria. Bladder catheterization was done on all the patients. Anuria was determined if patients secreted less than 4 ml of urine per hour. Oliguria was determined if patients secreted less than 21 ml of urine per hour. Anuria and oliguria had various duration which were or were not accompanyed by the elevated serum creatinine concentration. That is why all the patients were conditionally divided into 3 groups.

1) Patients with increased serum creatinine concentreation taking place more than 4 days (8);
2) Patients with increased serum creatinine concentration taking place less than 4 days (24);
3) Patients with nonprolonged anuria or oliguria and normal serum creatinine concentration (22).

Comparative groups were statisitically identical by age, sex, dehydration degree, period from outset of cholera to hospitalization and structure of pathogenetic and etiotropic therapy.

Results and discussion

The elevated serum creatinine concentration, which persisted meanly for 4.1± 0.32 days, was registered in 32 patients with severe course of cholera (59.3%).

The problem concerning with knowing the basic morphological cause of renal failure for cholera is important. In our time there are following notions: prerenal (functional) and renal (true) failure[2]. The patients with fuctional renal failure had no organic renal disorders and decreasing of diuresis occurs due to dehydration, arterial hypotension and hypovolemia. While functional renal disorders cause changes in the kidney's parenchyma Oliguria or Anuria reflect the development of the true renal failure.

The problem can be solved very quickly in the case of prerenal failure, when patients instead of anuria have no elevated serum creatinine concentration (group 3). However, this problem is very important when elevated serum creatinine concentration takes place (group 1 and 2). At the same time, differentiation between prerenal and renal failure for cholera has essential practical importance for the definition of treatment tactics and cholera prognosis.

Clinical and laboratory data allowed us to diagnose the true acute renal failure in group 1 and the prerenal failure in group 2. The diagnosis of acute (true) renal failure were based on: prolonged oliguria or anuria; high parameters of serum creatinine concentration and protracted creatinemia; ratio of serum creatinine concentration/the blood urea nitrogen value increasing elevated serum potassium concentration; anemia; actually similar osmolality of urine and blood serum.

However, it's worth while to note that the differenciation between prerenal and acute renal failure during cholera is possible only retrospectively or when the latter becomes considerably manifested. In other words, it is difficult to solve this problem and elaborate the tactics of treatment of patients in the early stages of

JK-Practitioner 1999; 6(1): 78-79

From Infectious Disease Department, Vinnitsa State Medical University, Ukraine (Kiritcheneko)

Received October 1998 Accepted 19888

Corespondence: Dr. Pavel D. Kiritchenko, PO Box 8105 (Glavpochtamt) Vittitsa 286050, Ukraine.

hospitalization. That is why taking into consideration the wide-known principle (it is better to prevent the disease than treat it) we elaborated the criterions of estimation of the acute renal failure risk in patients with cholera.

The estimation of acute renal failure risk in patients with cholera

Parameter	Number of points
1. Age above 60	2
2. Availability of severe chronic pathology (kidney diseases, diabetes mellitus, tuberculosis, hepatitis, tumors)	4
3. Serum postassium concentratin before treatment begining <3.6 mmol/l	5
4. Serum chloride concentrtion before treatment begining <95 mmol/l	4
5. Erythrocyte potassium concentration before treatment begining <70 mmol/l	7
6. Ratio serum creatinine concentration (mkmol/l) /blood urea nitrogen value (mmol/l) before treatment begining >30	3
7. Duration of anuria (by bladder catheterization data) >5 hours	6
8. Specific weight of first portions of urine <1015	6
9. Proteinuria in first portions of urine >0.3g/l	3
10. Number of leukocytes in first portions of urine >9	5
11. Availability of erythrocytes in first portions of urine > 9	3

In order to solve this problem 3 groups of patients had been compared by the anamnesis, clinical and laboratory parameters. Then we chose the parameters which significantly differed among groups. A probability value of less than 5% was considered statistically significant. The data was tested with the help of multifactor analysis of variance, so the role (%) of each factor in renal failure formation was determined. proceeding from the results of analysis of variance each factor obtained definite number of points. We used only parameters which could be obtained in the first 12-24 hours of hspitalization. The results of investigation are shown in talbe-1.

After testing the patients according to the scale mentioned above it turned out that hgih risk of acute (true) renal failure took place if the sum of all the points was more than 30. The risk was moderate if the sum was 20-30 and insignificant-if the sum was less than 20.

We consider that for the high risk of acute renal failure it is worth while to administer preparations improving renal haemocirculation (heparinum, euphyllinim, trental and others). Moreover, doctors should refrain from prescription of nephrotoxic remedies in such patients that concerns first of all with some kinds of antibiotic.

References:

1. Barua D., Greenough W. Cholera-Plenum Medical Book Company.: NY and London, 1992, 372p.
2. Klahr S. The kidney and body fluids in health and disease. Plenum Medicla Book Company.: NY and London, 1983; 448p.

Birth Weight in Relationship to Blood Groups

Birth weight is definitely influenced by prenatal and postnatal factors which range from hereditary, racial, genetic factors on one side to medical and obstetric disease of mother alongwith environmental and social factors on the other-side.[1] Relationship between blood groups like blood group O and A with some disease (peptic ulcer, pernicious anaemia, diabeties and gynecological diseases) is already known.[2] More recently babies with AB blood groups were shown to have least birth weight compared to other groups.[3] This interesting observation of possible role of blood group with birth weight has prompted us to further substantiate these findings.

The Present study has been conducted on 1138 singleton live born consecutive babies between January 1997 to March 1998 at Obstetric Hospital, Sher-i-Kashmir Institute of Medical Sciences, Srinagar. All the babies irrespective of their gestation, mode of delivery and antenatal problem (if any), have been included. Blood grouping of the mother and baby was done by standard test (Darmady).[4] Babies blood was obtained from umbilical cord immediately after birth and mother's blood group was repeated irrespective of whether she had done it antenally or not. Birth weight of babies was recorded within one hour of delivery using pan type spring balance (with an accuracy of 10 gms). Care has been taken with frequent checks of the weighing scale for its accurate measurements. The data collection has been made by only author and the findings were subjected to Chi-square and 't' test wherever applicable.

Present study showed that 37.43% mothers and 25.14% new borns belonged to blood group O and least frequent blood group to which mothers (9.22%) and babies (8.62%) belonged was AB blood group. The other two blood groups were almost equally distributed. The maximum mean birth weight was 2.99±.37 kgs among blood group B followed by 2.96±.4 kgs among blood group O. Significantly low mean birth weight of 2.49±.42 kgs was observed among babies with AB blood group ($p<.001$). Of the 1138 babies 60.6% (690) had similar blood group as their mothers and rest had dissimilar blood groups. However, mean birth weight was not significantly different. Between 67% to 73% babies with blood group AB and O were having birth weight <2.5 kgs compared to AB blood group where only 46% babies weighed more than 2.5 kg and the findings were statistically significant ($p<.001$).

The present study has revealed that AB blood group is not only least frequent blood group in Kashmiri female population but also has lower mean weight values. These findings are consistent with Nayak et al.[5] A varying degree of relationship between ABO blood groups with birth weight in the present study shows possible association between blood groups with one of the physiological parameter viz birth weight. Dissimilarity between blood group of mother and infant (ABO in compatibility) reported by Boethether[6] as the cause for this low birth weight does not seem to be the possiblility in the present study as there was not significant difference between mean birth weights of similar and dissimilar blood group. Since amongst the AB blood group, premature deliveries were negligible, therefore it may be concluded that relationship between AB blood group and birth weight needs a detailed and well controlled study before conclusion of role of blood groups as determinants of low birth weight is expressed.

TABLE IV: BLOOD GROUP DISTRIBUTION AND BABY WEIGHT.

		Birth Weight			
Blood group	1.5 kgs or less	1.55 - 2.5 kgs	2.55 - 3.5 kgs	3.55 kgs or more	Total
A	6(2.3%)	78 (300.16%)	161(62.16%)	14(5.4%	159
B	3(0.87%)	92(26.74%)	234(67.26%)	19(5.52%)	348
AB	11(12.79%)	34(39.53%)	37(43.02%)	4(3.80%)	105
O	4(0.6%)	105(24.84%)	305(71.21%)	12(2.83%)	426

$X^2 = 75.99$ $p<.001$

df = 9

Abida Ahmad, M.S.; Imtiyaz Ali Bhat, M.D.; Department of obstetrics (Abida) and Community Medicine (Bhat), SK Institute of Medical Sciences, Soura, India.

JK-Practitioner 1999; 6(1): 80

References:

1. K. Park. Park's Test Book of Social and Preventive Medicine. 14th Ed. (1194). Published by M/s Banarsidas Bhanotprem Nagar, Jabalpur 1994; p 321,
2. Hurkat PC, Agarwal VK. ABO blood group in relation to abortion. Jr of Obst & Gynae of India 1985; 35(3): 494-97.
3. Harkat PC, Agarwal VK. The ABO blood groupin relation to Abortions. Jr of Obst & Gynae of India 1985; 35(3): 494.
4. Darmady EM, Devenport SW. Haematological Technique. Ist Ed. (1963) Publisher J & Achurchill Ltd. p 225.
5. Nayak AH, Dalal AR. ABO blood groups and Birth weight. Ind Jr of Obst & Gynaecology 1992; 42(3): 314-316.
6. Boeltchor B, Hay AJ. An investigation of a proposed mechanism for infertility based on ABO, blood group in compatibility. Amr Jr of Obst & Gynae 1968; 100: 473.

Social Correlates of Neonatal Septicaemia

Neonatal septicaemia is a disease of infants who are less than one month of age and are critically ill having positive blood culture. The presence of clinical manifestation distinguishes this condition form transient bacteriemia seen in some healthy neonates. It can also be defined as bacteraemia in presence of signs and symptoms caused by microorganisms or their toxins in the circulation. It has also been described as a persistent or recurrent bacteraemia due to inability of body mechanisms to localise the infection giving rise to actual fulminant, sometimes protracted illness with a significant mortality. Neonatal septicaemia is one of the major causes of morbidity and mortality in developing countries and accounts for nearly half of the deaths in neonatal age in India. Timely diagnosis of neonatal sepsis and consequent start of treatment has a dramatic influence on prognosis of neonatal specticaemia.

A study was conducted in the department of Maternal Health Unit of Community Medicine and Neonatology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir from March 1995 to March 1996 with an aim to identify the epidemiological correlates of neonatal septicaemia among hospital born neonates.

Out of 228 deliveries conducted in the department of Community Medicine in Material Health Unit during the period, 150 pregnant women with predospsing factors (one or more than one) viz, premature rupture of membranes 24 hours, mucunium stained liquor, foul smelling liquor, maternal fever, prolonged labour, more than five vaginal examination, admitted in the maternal Health Unit of Sher-i-Kashmir Institute of Medical Sciences, Srinagar for deliveries, were studied during a time span of one year.

The socio economic factors like age of the mother, literacy, type of family, income, occupation and other obstetric correlates were studied which had direct impact on neonatal septicaemia.The socio-economic factors have a direct influence on overall status of the mother and thereby on any favourable outcome of the foetus. Septicaemic neonate thus similarly have direct relationship with the socioeconomical and environmental factors. High risk perinatal factors with low socio-economic profile has an direct impact on neonatal septicaemia. Illiteracy, low income, age at marriage and type of delivery had direct effect on birth of faetus, causing low birth weight and are thus prone to neonatal infections. Similarly associated medical illnesses of mothers, anaemia has effect on perinatal outcome, amounting to mortality and morbidity of neonates.

The disease was thus found to have a positive correlation with various epidemiological, obstetric and neonatal correlates viz; literacy rate, type of family, percapita income, maternal age, associated illness during pregnancy like anemia, PET, diabetes, APH and infective hepatitis, and predisposing factors like premature rupture of membranes (PROM) for 24 hours, fever, prolonged labour and number of vaginal examination.

This study revealed an incidence rate of (22.66%) of neonatal septicaemia which is quite high among these hospital born neonates and a mortality rate of 33.35%. The incidence of neonatal sepsis in our study was high as compared to other studies conducted in various developing countries. This could be because we had selected those mothers only who were having predisposing factors. About 85% were illiterate giving birth to 24(70.58%) of septicaemic neonates having a significant relationship between parenteral illiteracy and neonatal sepsis. This is statisitcally also significant. About 88(55.33%) mothers belonged to joint families giving birth 67(46.67%) of neonatal sepsis which is also statistically significant. About 96(64.00%) mothers belonged to family with a percapita income of Rs. 1000/- giving rise to 22(64.71%) of neonatal aspsis which is again statistically significant. About 122 (81.34%) mothers belonged to the age group of 20-30 years giving birth to 26(75.85%) having highest degree of correlation coefficient. About 70(46.67%) (Table-6) of mothers were primies giving birth to 50(33.33%) of neonatal sepsis followed by gravida two and multipara[2]. About 11(7.33%) mothers had associated illness like anaemia, PET, diabetes, infective hepatitis and APH. All 150 mothers had predisposing factors present. About 30(20.99%) mothers had predisposing factors like PROM 24 hours. 17(11.35%) had muconium stained liquor. 10 cases (6.66%) had maternal pyrexia, 29 cases (19.33%) had prolonged labour and 64(42.66%) had repeated vaginal examination.

The disease was thus found to have a positive correlation with various epidemiological, obstetric and neonatal correlates viz; literacy rate, type of family, percapita income, maternal age, associated illness during pregnancy like anemia, PET, diabetes, APH and infective hepatitis, and predisposing factors like premature rupture of membranes (PROM) for 24 hours, fever, prolonged labour and number of vaginal examination.

The socio-economical factors have a direct influences on over all status of the mother and thereby on any favourable or unfavourable outcome of the foetus, Septicaemic neonates thus similarly have a direct relationship with the socio-economic status of the mother. Stress is to be made on age at marriage, literacy level, spacing and health education regarding the delivery and care of the neonate, the epidemiological correlates having septicaemia should be delineated.

Khalida Hakeem, MD; Nighat Chiloo, MCH; Masood-ul-Hassan, M.Ch.
Department of Community Medicine SKIMS, Soura, Srinagar (J&K) India
JK-Practitioner 1999; 6(1): 81-82

Further Reading:

1. Dunhan ED. Septicaemia in new born, Amer J Dis Child 1933; 45: 229.
2. Mukherjee S et al and Biswas S. Birth weight and its relatinship to gestation period, sex, maternal age, parity and socioeconomic status. J.I. Med. Association, 1959; 32(10).
3. Kathleen Camay Beutow MD, Baltimore MD, S. Wayne Klein MD and Rosemary, Nordflesa. The characteristics, treatment and prevention of septicaemia in premature infants. Am. Jr. of Dis Child July 1965; 110: 29-40.
4. Gotoff S.P and Behraman RE, Neontal Septicaemia. Jr. of Paediatrician, Jan. 190; 143-152.
5. Saroj Pachauri, Marwash SM and Raso NSN. A multifactorial approach to the study of factors influencing birth weight in the urban community of New Delhi. Ind. J Med Res 1971; 10(3).
6. Santosh K Bhargava, Vijay Bhargava, Sudershen Kumari, Shants Madhavan and Shanti Gosh. Birth weight, gestational and maternal factors in low birth weight babies. Ind. Paeds 1977; 12(2).
7. Mehrotra N, Kumar A, Chansoniam, Koul K K, Neonatal sepsis correlation of maternal and neonatal factors to positive bacterial cultures. Ind. Paediatrics. 1985, 22: 275-280.
8. Theodore Kamaldass, Abel R and Sampath Kumar V. Epidemiological Correlates of low birth weight in rural Tamil Nadu. Ind. Paed. 1992; 50: 299-300.
9. Dhar GM, Shah GN, The influence of socioeconomic and obstetric correlates on hospital born neonates. Ind. J Mat. Child 1994; 5(6): 55-59.

A Study on Nutritional Status of Elderly Population in the Age Group (60-75 years) in Srinagar City

An aged person is not merely an old man but presents as Structural, functional chemical, metabolic, nutritional and psychological characteristics peculiar to Sensescence which is continuous, gradual and hardly discernable except by contrasting studies made at different intervals of life span[1].

The exact borderline between the physiology of aging and the pathology of aging is frequently indistinguistable[2].

Different risk factors for poor nutritional status have been identified which are inapropriate food intake, poverty, isolation, limited literacy, dependence and disability, acute chronic diseases or conditions, medication use and advanced age[3]

Major indicators of poor nutritional, status in elderly people are significantly low or high weight for height, significant reduction in serum albumin, decline in functional status, inappropriate food intake, reduction in midarm circumference, decrease or increase in skinfold measurement and nutrition related disorders e.g. osteoporsis, osteomalacia, folate deficiency, Vitamin B_{12} deficency, pressure sores[3].

With the improvement in the standards of living and a steady economic affluence resulting in better nutrition and health care, the elderly population in the State of Jammu & Kashmir is ever on the increase. No systematic study has been performed to assess the nutritional intake of this group of the population in our State. The present study addresses the preliminary observations on the nutritent intake and basic blood parameters suggestive of the nutritional status of the subjects, in a random cohot of this population group.

Seventy five randomily selected elderly subjects (aged 60-75 years) coming to the saddar treasury and Additional treasury and State Bank of India to collect their pension and other dues without any chronic disease in the months of Febuary to April, 1997 constituted the subjects of the study. All the subjects were interveiwed and findings regarding symptoms of any nutritional deficiency were recorded on predefined questionaire developed as per WHO guidelines[4].

Exact address of the subjects was noted down and dietary survey was carried out by personally visiting there homes. Dietary intake was recorded by the 7-day weighment method and the nutritent intake of the subjects were calculated with the help of nutritive value of Indian foods[5]. Blood samples were analysed for haemoglobin by filter paper technique, cholesterol by Zlatkis method and serum calcium by colorimetric method[6]. The data are represented as mean±SD. Statistical analysis was performed employing students T-test for independent samples. A P value of (< 0.05) was considered significant.

The subjects studied consisted of 50 males and 25 females with ages ranging from 60 to 75 years. The height of the males ranged from 142 cm - 185 cm (mean SD 1611±10.2). Where as mean height of females was 150.0 8.2 cm (range 135 cm to 165 cm). The weight of the male subjects ranged from 40 kg to 92 Kg (mean 59.9±10.2 kg) whereas that of the females ranged from 40Kg to 66 kgs (mean 52.7±7.9 kg) the height and weight of males was significantly more than that of females ($P<0.01$).

21% Males and 9% of females had history of peptic ulcer, 3% Males and 6% females had bleeding gums which could have resulted in low Hb levels.

The mean HB% levels in males were 12.01±1.5 (range didn't differ significantly from the level in females 10.3±1.1 (range 9.0 to 13.9) $P>0.01$.

The mean Intake of Proteins, Calories, Iron and Vitamin A, Vitamin C & B2 were significantly higher in males as compared to females.

Mean cholesterol level in males 242.26±38.10mg% (range 234.40 to 250.22) & in females 233.02±16.24 (range 222.08 to 245.28) with no statistically significant difference between the two groups ($P>0.05$).

The mean values of serum cholestrol showed a gradual increase with increasing age. It is possible that any rise in serum cholestrol values observed with increasing age could be related more to accompaning dimunition in physical activity than age. More meat consumption & fats consumption can be related to high cholesterol level.

Mean serum Calcium levels in males was 8.1±0.9 mg% (range 6.9-9.99) & that in females 7.9±0.8 (range 6.6 to 9.9 mg/100ml) with no statistically significant difference between the two groups ($P>0.01$).

Our study has shown that the elderly in Kashmir have a higher weight for height as compared to the normal ICMR standards. Such a paradox could be attributed to sedentary life style because energy in takes of all the subjects was lower than RDA. The mean in take of proteins was on higher side because of greater consumption oof meat etc. which is usual for the winter months in Kashmir. It may also reflect a good care imparted to the nutritional requirements of elderly by the youngesters at home. The mean heamoglobin and calclum levels for both the sexes were found to be below the normal standards which can be attributed to less intake of green leafy vegetables and fresh fruits & vegetables, low serum calcium levels can be attributed to less dietary intakes of vitamin D. It is suggested that elderly people should be educated about the proper selection of food items and good amounts of calcium and vitamin D should be utilized so that there is no withdrawal of calcium from bones for maintenance of serum calicum levels & prevent further damages to bones in old age. This is especially true of females as bone resorption and hence osteoporosis is a fequent accompaniment of the hypoestrogenic state consequent upon menopause. Vitamin D supplements and exposure to sun are further advocated.

Yasmeen Khan
Lecturer, Deptt. of Home Sciences
University of Kashmir,
Hazratbal, Srinagar.
JK-Practitioner 1999; 6(1):82-83

References:

1. Nirmal K Murhty et al (1986) Biochemical changes in Elderly women beloging to low socio-economic group. The Indian journal of Dietetics (1986) pp. 23, 31.
2. Frank A.S. & Hedegard (1973) Geriatric dentisty. J.B. liggpincoit Phyladelphia pp. 23-30.
3. Ham. J. Richard; Sloane D. Phillip. Primary care geriatrics Copyright (1997) by Mosby Year Book Philadelphia Portiand. pp. 108-114.
4. Jelliffe D.B. (1966). The assessment of the Nutritional Status of the Community (p.p. 10-30) World Health Organisation, Geneva.
5. Gopalan C Rama; B.V. Bala Subramunium Nutritive value of Indian Food p.p. 27 (1985) N.N. Hydrabad.
6. Bernard L. Oser (1979) Estimation of Srum Calcium; Physiological Chemsitry 4th ed P.P. 1133-1134. Tata Mcgraw Hill Publishing Co. Ltd., New Delhi.

1998 Management Recommendations for Sexually Transmitted Diseases

Bilal A. Malik, MD; Gurpreet Singh, MD; Tanveer Mir, MD, FACP;

Guidelines for Management of Sexually Transmitted Diseases:

Sexually transmitted diseases (STD's) comprise a significant percentage of all infectious disease. They mostly affect young people and lead to significant morbidity. Recently the Center for Disease Control (CDC) published recommendations for management of STD's developed by CDC staff members after consultation with experts on the subject. In the original form they are published in the mortality and morbidity weekly report (MMWR) Jan 23, 97/ vol. 47/ No. RR-1.

In this article we attempted a summary of these recommendations with stress on the treatment, follow up and special circumstances like pregnancy and HIV infection. For detailed information the original recommendations or the various references in the MMWR may be consulted.

Diseases Characterized by Genital ulcers:

Chancroid:

Recommended regimens:

1. Azithromycin 1gm PO single dose or
2. Ceftriaxone 250mg IM in a single dose or
3. Ciprofloxacin 500mg PO twice a day for 3 days or
4. Erythromycin base 500mg PO four times a day for 7 days

Other Management Considerations: - Patients should be tested for Syphilis and HIV at diagnosis and 3 months later, if initially negative.

Follow up: Patients should be re-examined 3-7 days after initiation of therapy. If no clinical improvement is evident consider the following

a) diagnosis is not correct
b) the patient is co-infected with another STD
c) the patient is infected with HIV
d) treatment was not taken as instructed
e) the H. Ducreyi strain is resistant.

Larger ulcers may require more than 2 weeks to heal. Buboes should be drained.

Management of Sexual partners: Sexual partners should be treated regardless of symptoms of the disease, if they had sexual contact during the 10 days preceding the symptoms.

Pregnancy: Safety of Azithromycin has not been established. Ciprofloxacin is contraindicated. No adverse effects of chancroid on the fetus have been reported.

HIV Infection: Patients may require longer courses, 7 day oral regimen of erythromycin is recommended.

Genital Herpes:

Topical medications are discouraged.

Treatment Regimens:

First Episode :

1. Acyclovir 400mg PO three times a day for 7-10 days or
2. Acyclovir 200mg PO five times a day for 7-10 days or
3. Famciclovir 250mg PO three times a day for 7-10days or
4. Valacyclovir 1 gm PO twice a day for 7-10 days

Recurrent Episode:

1. Acyclovir 400mg PO three times a day for 5 days or
2. Acyclovir 200mg PO five times a day for 5 days or
3. Acyclovir 800mg PO twicea day for 5 days or
4. Famciclovir 125mg PO twice a day for 5 days or
5. Valacyclovir 500mg PO twice a day for 5 days

Daily Suppressive therapy:

Indication: Frequent recurrences more than 6 episodes a year. After 1 year of continuos therapy, discuss the discontinuation of therapy with the patient. Suppressive therapy reduces but does not eliminate chances of asymptomatic viral shedding.

Recommended regimens:

1. Acyclovir 400mg PO twice a day or
2. Famcicilovir 250mg PO twice a day or
3. Valacyclovir 250mg PO twice a day or
4. Valacyclivir 500mg PO once a day or
5. Valacyclivir 1000mg PO once a day

Valacyclovir and Famciclovir are comparable to Acyclovir and provide ease in administration. For severe disease necessitating hospitalization such as disseminated infection, pneumonitis, hepatitis or CNS involvement.

Recommended regimen: Acyclovir 5-10mg/kg IV 8hrly for 5-7days or until clinical resolution is attained.

Management of Sex partners:

Asymptomatic sexual partners should be evaluated and counseled. Symptomatic sexual partners should be treated as usual.

Pregnancy:

Safety of acyclovir and velacyclovir has not been established. The first episode may be treated with oral acyclovir. Life threatening infection should be treated with intravenous acyclovir.

Perinatal:

The risk of perinatal transmission is highest (30-50%) among women who acquire herpes near the time of delivery.

At the onset of labour, all women should be examined and questioned for symptoms of genital herpes. Those wihout the signs and symptoms may be delivered vaginally. Abdominal delivery does not completely eliminate the risk of herpes in the neonate.

Infants exposed to HSV during birth should be followed carefully, routine use of acyclovir in asymptomatic exposed infants is not recommended.

Neonatal Herpes is treated with acyclovir 30-60mg/kg/day for 10-21 days.

Infants: Asymptomatic infants should be watched carefully. Symptomatic acyclovir 30-60mg/kg/day IV 10-21 days.

HIV: Disease is usually severe and prolonged.

Recommended regimens:

1. Acyclovir 400mg 3-5 times a day until resolution.
2. Famciclovir 500mg twice a day till clinical resolution.

JK-Practitioner 1999, 6(1): 84-91
From the department of Medicine Nassau County Medical Centre, Est Meadow New York (Malik, Gurpreet, Tanveer)
Received November 1998 Accepted December 1998

Persistent Disease/ Resistant Patients:

1. Foscarnet 40mg/kg 8hrly until resolution with topical cidofovir gel, 1% every day for 5 days

Granuloma Inguinale (Donovanosis):

Treatment Regimens:

1. Trimethoprim- sulphamethaxole, 1 DS PO, twice a day minimum for 3weeks or
2. Doxycycline 100mg PO twice a day for minimum of 3 weeks Therapy should be continued until all lesions have healed.

Alternative Regimens:

1. Ciprofloxacin 750mg PO Twice a day for a minimum of 3 weeks or
2. Erythromycin base 500mg orally four times a day for a minimum of 3 weeks.

For all the above-mentioned regimens, Gentamycin 1mg/kg every eight hours should be considered if lesions do not respond within the first few days of therapy.

Follow up:

Clinically until signs and symptoms of the disease have resolved.

Management of Sex Partners:

Should be examined and treated if the sexual contact was within 60 days or clinical signs of the disease are detected.

Pregnancy: Use erythromycin regimen and strongly consider addition of parental aminogylcoside.

HIV: Same regimen, strongly consider adding aminoglycoside.

Lymphogranuloma Venereum:

Recommended regimen:

1. Doxycycline 100mg twice a day 21 days

Alternative regimen:

1. Erythromycin base 500 mg four times a day 21 days.

Follow up:

Clinically until signs and symptoms have resolved.

Management of Sexual partners:

Sexual partners should be treated if they had sexual contact with the patient during 30 days preceding onset of symptoms

Pregnancy:

Treat with a regimen of erythromycin

HIV:

These patients may require prolonged therapy

Syphilis:

Primary and Secondary Syphilis :

Recommended regimens:

Adults	benzathine penicillin G 2.4 million units IM single dose
Children	benzathine penicillin G 50,000 units/kg IM upto an adult dose of 2.4 million units in a single dose.

Other management considerations:

Test for HIV at diagnosis, retest in 3 months if negative. Unless clinical signs and symptoms of neurological or ophthalmic involvement are present, spinal tap is not recommended for routine evaluation.

Follow up:

Re-examine clinically and serologically at both 6 and 12 months, more frequently if follow up is uncertain. Persistent signs and symptoms or recurrence or sustained fourfold increase in titers signify failed treatment or re-infection . Patients should be re-evaluated for HIV infection and should be re-treated. Perform spinal tap unless re-infection is certain.

Failure of the test titers to decline fourfold within 6 months therapy identifies patients at risk of treatment failure. Optimal treatment is uncertain , needs additional clinical and serologic follow up or re-treatment is recommended with Benzathine pencillin G 2.4 million units IM weekly for 3 weeks if additional follow up is uncertain.

Special conditions :

Penicillin Allergy;

Non pregnant:

Recommended regimen:

1. Doxycycline 100mg PO twice daily 2 weeks
2. Tetracycline 500mg PO 4 times a day 2 weeks

Alternative:

1. Erythromycin 500mg PO four times a day for two weeks
2. Ceftriaxone 1 gm Intravenous for 8-10 days

Pregnancy:

Desensitization

Latent Syphilis:

Adults: Early latent syphilis- benzathine penicillin G 2.4 million units as a single IM dose

Late latent syphilis or latent syphilis of unknown duration- Benzathine Pencillin G 7.2 million units total in 3 divided doses at 1week intervals.

Children: with normal CSF, Early latent syphilis-Benzathine Penicillin G 50 000 units/kg IM upto 2.4 million units in a single dose.

Late latent syphilis or latent syphilis of unknown duration- Benzathine Penicillin G 50 000 units/kg IM upto 2.4 million units, 3 doses at 1 wk intervals

Management considerations:

Evaluate for tertiary disease

Prompt CSF examination

Follow up:

Non-treponemal serologic tests repeated at 6, 12, 24 months, evaluate for neurosyphilis and treat appropriately if a) titers increase fourfold b) Initially high titer (>1:32) fails to decline fourfold in 12-24 months or c) Signs and symptoms develop.

Penicillin Allergy:

Non-pregnant patients- Doxycycline 100mg twice a day OR Tetracycline 500mg PO 4 times a day for 2 weeks if duration of infection known to be less than 1 year otherwise 4 weeks.

Pregnancy: Desensitization

Tertiary Syphilis:

Recommended regimen:

Benzathine penicillin G 7.2 million units total, 2.4 million units IM 3 doses at 1 week intervals

Penicillin Allergy:

Same as late syphilis

Pregnancy: Desensitization

Neuro-Syphilis:

Recommended regimen:

Aqueous crystalline Penicillin G 18-24 million units/day , 3-4 million units IV 4 hourly 10-14 days

Alternative:

1. Procaine penicillin 2-4 million units IM a day plus probenecid 500mg PO 4 times a day, both for 10-14 days.
2. Some administer benzathine penicillin 2.4 million units IM after completion of treatment for neurosyphilis.

Follow up:

CSF every 6 months until cell count is normal, also follow

CSF VDRL and

CSF protein. If cell count not decreased at 6 months or CSF not entirely normal in 2 years Retreat

Penicillin Allergy:

Desensitize/ manage in consultation with an expert

Pregnancy:

Desensitization

Syphilis in HIV Infected Patients:

Primary and secondary syphilis:

Benzathine penicillin G 2.4 million units IM OR Some experts recommend benzathine penicillin G 2.4 million units IM 3 doses

Follow up:

Clinically and serologically at 3,6,9,12 and 24 months. Some experts recommend CSF at 6 months. Retreat if the above criteria for re-treatment are met. If the titers do not decrease fourfold within 6-12 months, retreat with benzathine penicillin G 2.4 million units weekly 3 doses.

Latent Syphilis in HIV:

Benzathine penicillin G 2.4 million units wkly 3 doses

Follow up:

Clinically and serologically at 6,12,18 and 24 months. If clinical symptoms develop or titer increases 4 fold, repeat CSF examination. If in 12-24 month titer fails to decline 4 fold repeat CSF examination.

Syphilis during pregnancy:

Penicillin regimen appropriate for the setting

Follow up:

Repeat serological test in 3rd trimester and at delivery, may be checked monthly in women at high risk for reinfection or in geographic areas in which prevalence of syphilis is high.

Penicillin Allergy:

No proven alternatives, desensitization is recommended

Tetracycline and doxycycline usually not used. Erythromycin should not be used as it does not reliably cure an infected fetus. Data on azithromycin and ceftriaxone is insufficient.

Congenital Syphilis:

Infants:

1. Aqueous crystalline penicillin 100 000-150 000 units/kg/day administered as 50 000 units/kg/dose IV 12 hourly for first 7 days of life and every 8 hourly thereafter for total of 10 days or
2. Procaine penicillin G 50 000 units /kg/dose IM once a day 10 days

Older infants/children:

Congenital/neurosyphilis- aqueous penicillin G 200, 000-300,000 units/kg/day IV, administered as 50, 000 units/kg every 4-6hrly for 10 days

Follow up:

Examination and serology every 2-3 months till serology becomes non-reactive or the titer decreases fourfold. Repeat CSF every 6 months until normal, if initially abnormal.

Penicillin Allergy:

No proven alternatives are available for treating neurosyphilis, congenital syphilis, or syphilis in pregnant women. Also recommended whenever possible in HIV infected patients.

Disease characterized by urethritis and cervicitis :

Urethritis:

Confirmation of urethritis a) mucopurulent or purulent discharge
b) gram stain of urethral secretions >5 wbc per oil immersion
c) positive leukocyte esterase test or >10 wbc per HPF on first void sample

Non Gonococcal urethritis:

Recommended regimens:

1. Azithromycin 1 gm PO in a single dose or
2. Doxycycline 100mg PO twice a day 7 days

Alternative regimens:

1. Erythromycin base 500mg PO four times a day 7days or
2. Erythromycin succinate 800mg four times a day 7 days or
3. Ofloxacin 300mg twice a day 7 days or
4. Erythromycin base 250mg PO four times a day 7 days or
5. Erythromycin ethylsuccinate 400mg PO four times a day 14 days

Follow up:

Patients advised to return if symptoms recur or persist, abstain from sexual intercourse until therapy is completed.

Sex Partners:

All sex partners within the preceding 60 days should be referred for evaluation and treatment.

Recurrent or Persistent Urethritis:

Recommended regimens:

1. Metronidazole 2gm PO in a single dose plus Erythromycin base 500mg PO four times a day 7 days or
2. Erythromycin ethylsuccinate 800mg PO four times a day /7 days

HIV Infection:

Treatment regimens are the same as above

Mucupurulent Cervicitis:

The results of sensitive tests for C. trachomatis or N. gonorrhea should determine the need for treatment, unless likelihood of infection is high or patient is not likely to return for follow up.

Follow up:

If symptoms persist instruct to return for reevaluation and abstain from sexual intercourse even if they have completed the therapy.

Sex partners:

Partners should be notified, examined and treated for STD identified or suspected. Abstain from sexual intercourse until they are cured or until the therapies are completed usually 7 days.

Chlamydial Infection:

Recommended regimens:

1. Azithromycin 1 gm PO in a single dose or
2. Doxycycline 100 mg twice a day 7 days

Alternative regimens :

1. Erythromycin base 500mg PO four times a day for 7 days or
2. Erythromycin ethylsuccinate 800 mg PO four times a day for 7 days or
3. Ofloxacin 300mg PO twice a day 7 days

Follow up:

Retest for Chlamydia only if symptoms persist or re infection is suspected. Abstain from sexual intercourse for 7 days after single dose or completion of the 7 day regimen.

Sex Partners:

Sex partners are evaluated , tested and treated if they had sexual intercourse during the 60 days preceding the onset of symptoms in the patient.

Pregnancy:

Recommended regimens:

1. Erythromycin base 500mg PO four times a day 7 days OR
2. Amoxicillin 500mg PO three times a day 7 days

Alternative regimens:

1. Erythromycin base 250mg PO four times a day 14 days or
2. Erythromycin ethylsuccinate 800mg PO four times a day 7 days or
3. Erythromycin ethylsuccinate 400mg PO four times a day 14 days or
4. Azithromycin 1 gm PO in a single dose

HIV infection:

Same treatment as non HIV patients.

Chlamydial infection in Infants:

Neonatal ocular prophylaxis with silver nitrate solution or antibiotic ointments do not prevent transmission from mother to infant.

Opthalmia neonatorum caused by Chlamydia:

Erythromycin 50mg/kg/day PO divided into four daily doses for 10-14 days

Follow up:

It is recommended to determine resolution

Mothers and their sex partners:

Should be evaluated and treated.

Infant pneumonia caused by Chlamydia:

1. Erythromycin 50mg /kg/day PO divided into four doses daily for 10-14 days

Follow up:

Recommended to determine resolution of pneumonia

Infants born to mothers who have Chlamydial infection:

Prophylactic treatment is not recommended, infants should be monitored to ensure proper treatment if infection develops.

Chlamydial infection in children:

Recommended regimens:

Children < 45kg:	1. Erythromycin 50mg/kg/day PO divided into 4 doses 10-14 days
45kg but <8yrs:	1. Azithromycin 1 gm PO in a single dose or 2. Doxycycline 100mg PO twice daily 7 days
Children >8yrs:	1. Azithromycin 1 gm PO in a single dose or 2. Doxycycline 100mg PO twice a day for 7 days

Follow up:

Cultures are necessary to ensure that the treatment has been effective

Gonoccocal Infection:

Uncomplicated Gonococcal infections of Cervix, Urethra and rectum:

Recommended regimens:

1. Cefexime 400mg single dose or
2. Ceftriaxone 125mg IM single dose or
3. Ciprofloxacin 500mg PO single dose or
4. Ofloxacin 400mg Po single dose or
5. Azithromycin 1gm PO single dose or
6. Doxycycline 100mg PO twice a day for 7 days

Alternative regimens:

1. Spectinomycin 2gm IM single dose

Single dose Cephalosporin regimens:

1. Ceftizoxime 500mg IM, Cefotaxime 500mg IM.
2. Cefotetan 1gm IM, Cefoxitin 2gm IM with Probenecid 1 gm/PO.

Single dose quinolone regimens:

1. Enoxacin 400 mg PO, Lomofloxacin 400mg PO and
2. Norfloxacin 800mg PO.

Uncomplicated Gonococccal Infection of Pharynx:

Recommended regimens:

1. Ceftriaxone 125mg IM in a single dose or
2. Ciprofloxacin 500mg PO in a single dose or
3. Ofloxacin 400mg PO in a single dose plus Azithromycin 1 gm PO in a single dose or
4. Doxycycline 100mg PO twice a day for 7 days

Follow up:

Patients with persistent symptoms should be evaluated by culture and testing for antimicrobial sensitivity.

Treatment of Sex partners:

All sex partners of the patient should be evaluated and treated if the last sexual contact was within 60 days of onset of symptoms or diagnosis.

Sexual intercourse should be avoided until therapy is completed and the symptoms resolve.

Pregnancy:

Recommended regimen:

Cephalosporin regimens are the treatment of choice.

Alternative:

Spectinomycin 2gm IM in a single dose

HIV Infection:

Same regimens as in HIV negative

Gonococcal Conjunctivitis:

Recommended regimen:

Ceftriaxone 1gm in a single dose and lavage with saline once

Sex partners:

Evaluation and treatment of sex partners is recommended

Disseminated Gonococcal Infection:

Hospitalization is recommended for initial therapy. meningitis and endocarditis should be excluded. Presumptive treatment for Chlamydia begun unless excluded by appropriate testing.

Recommended initial regimen:

1. Ceftriaxone 1gm IM or IV every 24 hrs

Alternative regimens:

1. Cefotaxime 1gm IV every 8hrs or
2. Ceftizoxime 1gm IV every 8hrs or for β-lactam allergy

1. Ciprofloxacin 500mg IV every 12 hrs or
2. Ofloxacin 400mg IV every 12 hrs or
3. Spectinomycin 2gm IM every 12 hrs

All regimens should be continued for 24-48 hrs after improvement begins then switched to one of the following to complete a full week of therapy :

1. Cefixime 400mg PO twice a day or
2. Ciprofloxacin 500mg PO twice a day or
3. Ofloxacin 400mg PO twice a day

Management of Sex Partners : should be evaluated and treated

Gonococcal Meningitis and Endocarditis:

Recommended initial regimen :

1. Ceftriaxone 1-2gm Intravenous every 12 h For meningitis 10-14 days

For endocarditis at least 4 weeks

Gonococcal Infection in Infants:

Ophthalmia neonatorum:

Recommended regimen:

Ceftriaxone 25-50mg/kg IV or IM in a single dose, maximum 125mg

Management considerations:

Topical antibiotic therapy is inadequate and unnecessary if systemic therapy is given.

Simultaneous Chlamydial infection should be considered if the response is not satisfactory

Ceftriaxone should be administered cautiously to premature and hyperbilirubinemic infants

Follow up:

Infants with gonococcal ophthalmia should be hospitalized and evaluated for disseminated infection. Some pediatricians continue antibiotics till cultures are negative at 48-72hrs

Mothers and their Sex partners:

Should be evaluated and treated

Disseminated Gonococcal infection and Gonococcal scalp abscesses in Newborns:

Recommended regimens:

1. Ceftriaxone 25-50mg/kg/day IV or IM in a single dose for 7 days , for 10-14 days if meningitis is documented or
2. Cefotaxime 25mg/kg IV or IM every 12 hrs for 7 days, for 10-14 days if meningitis is documented

Prophylactic treatment for infants whose mothers have Gonococcal infection:

Recommended regimen:

1. Ceftriaxone 25-50 mg/kg/day IV or IM, not to exceed 125mg,in a single dose.

Mother and infant should be tested for Chlamydial infection.

Follow Up:

Not required

Mothers and their sex partners:

Should be evaluated and treated

Gonococcal Infection in children:

Children weighing >45 kg should be treated with one of the regimens recommended for adults. Quinolones are not approved for use in children .

Children <45 kg with uncomplicated vulvovaginitis, cervicitis, urethritis, pharyngitis or proctitis :

Recommended regimen:

1. Ceftriaxone 125mg IM in a single dose

Alternative:

1. Spectinomycin 40mg/kg (max:2gm) IM in a single dose

Children <45 kg with bacteremia and arthritis:

1. Ceftriaxone 50mg/kg (max : 1gm)IM or IV in a single dose daily for 7 days

Children >45kg with Bacteremia or arthritis:

1. Ceftriaxone 50mg/kg (max : 2gm) IM or IV in a single dose daily for 10-14 days

Follow up:

Unnecessary if ceftriaxone is used. If spectomycin is used a culture is necessary to ensure the effectiveness of treatment

All children infected with gonococcus should be evaluated for syphilis and Chlamydia

Ophthalmia Neonatorum Prophylaxis:

Recommended regimens:

1. Silver nitrate 1% aqueous sol in a single application or
2. Erythromycin 0.5% ophthalmic ointment single application

   or
3. Tetracycline ophthalmic ointment 1% in a single application

Disease Characterized by Vaginal Discharge:

Bacterial Vaginosis:

Non Pregnant Women:

Recommended regimens:

1. Metronidazole 500mg PO twice a day for 7 days or
2. Clindamycin cream 2%,one full applicator(5g) intravaginally at bed time for 7 days or
3. Metronidazole gel 0.75%, one full applicator(5g) intravaginally twice daily for 5 days

Alternative regimens:

1. Metronidazole 2g PO in a single dose or
2. Clindamycin 300mg PO twice a day for 7 days

Follow up:

Unnecessary if symptoms resolve

Sex partners:

Routine treatment not recommended

Pregnancy:

High risk women: who have history of preterm delivery, should be screened at the earliest part of second trimester.

Recommended regimens:

1. Metronidazole 250mg PO three times a day for 7 days or
2. Clindamycin 300mg PO twice a day for 7 days

Low risk pregnant women:

who do not have history of preterm delivery

Recommended regimens:

1. Metronidazole 250mg PO three times a day for 7 days

Alternative regimens:

1. Metronidazole 2g PO in a single dose or
2. Clindaamycin 300mg PO twice a day for 7 days or
3. Metronidazole gel 0.75% One full applicator (5g) intravaginally twice a day for 5 days

Trchomoniasis:

Recommended regimen:

1. Metronidazole 2gm PO in a single dose

Alternative regimen:

1. Metronidazole 500mg twice a day for 7 days

Follow up:

Not necessary for patients who become Asymptomatic.

Treatment failure:

Metronidazole 500mg twice a day for 7 days. If treatment failure occurs repeatedly – Metronidazole 2g once a day for 3-5 days

Sex partners:

They should be treated. Avoid sex until cured.

Allergy, Intolerance or adverse reactions to Metronidazole:

Effective alternatives not available, managed by desensitization

Pregnancy:

Metronidazole 2g in a single dose

HIV infection:

Same treatment as HIV negative

Vulvovaginal Candidiasis:

Recommended regimens:

Intravaginal agents:

1. Butaconazole 2% cream 5g intravaginally for 4 days or
2. Clotrimazole 1% cream 5g intravaginally for 7-14 days or
3. Clotrimazole 100mg vaginal tablet for 7 days or
4. Clotrimazole 100mg vaginal tablet, two tablets for 3 days or

5. Clotrimazole 500mg vaginal tablet , one tablet in a single dose or
6. Miconazole 2% cream 5g intravaginally for 7 days or
7. Miconazole 200mg vaginal suppository, one for 3 days or
8. Miconazole 100mg vaginal suppository, one for 7 days or
9. Nystatin 100,000 unit vaginal tablet, one tablet for 14 days or
10. Tioconazole 6.5% ointment 5g intravaginally in a single application or
11. Terconazole o.4% creams 5g intavaginally for 7 days or
12. Terconazole 0.8% cream 5g intravaginally for 3 days or
13. Terconazole 80mg vaginal suppository, one suppository for 3 days

Oral Agent:

1. Fluconazole 150mg oral tablet, one tablet in a single dose

Vulvuvaginal vaginitis in uncontrolled Diabetes or with less susceptible fungus like Candida glabrata:

Longer duration 10-14 days with either topical or oral azoles

Alternative Regimen:

Oral azoles are as effective as topical agents but their systemic toxicity limits their use

Follow up:

Return for follow up only if symptoms recur

Sex Partners:

Treatment of sex partners is not recommended, but should be considered for women who have recurrent infection

Pregnancy:

Only topical azole therapy should be used, many recommend it for 7 days

HIV Infection:

Questionable increased incidence of vulvovaginitis, same regimens used

Recurrent Vulvovaginal Candidiasis:

Four or more symptomatic episodes annually

Recommended regimens:

Initial intensive regimen for 10-14 days followed by a maintenance regimen for 6 months. Maintenance Ketoconazole 100mg PO once a day for 6 months reduces the frequency of the episodes

Follow up:

Regular follow up evaluations to monitor the effectiveness of therapy and the occurrence of side effects

Sex partners:

Routine treatment unnecessary, considered for partners who have symptomatic balanitis or penile dermatitis

HIV Infection:

Management same as HIV negative women

Pelvic Inflammatory Disease (PID):

Criteria for Hospitalization :

1. Surgical emergencies like appendicitis cannot be excluded
2. Patient is pregnant
3. Patient does not respond clinically to oral therapy
4. Patient is unable to follow or tolerate outpatient regimen
5. Patient has severe illness nausea, vomiting or high fever
6. Patient has tubo- ovarian abscess or
7. Patient is Immunodeficient

Parental therapy A:

1. Cefotetan 2g IV every 12 hrs or
2. Cefoxitin 2g IV every 6 hrs plus doxycycline 100mg IV/PO 12 hrly Parenteral therapy may be discontinued 24 hrs after a patient shows clinical improvement, and oral therapy with doxycycline 100mg PO twice a day continued for 14 days.

Parenteral Therapy B:

1. Clindamycin 900mg IV every 8 hrs plus gentamycin loading dose IV or IM 2mg/kg followed by 1.5mg/kg every 8 hrs Parenteral therapy may be discontinued 24 hrs after a patient shows clinical improvement, continuing oral therapy in the form of doxycycline 100mg twice a day or clindamycin 450mg four times a day to complete a total of 14 days

Alternative parental regimens:

1. Ofloxacin 400mg IV every 12 hrs plus metronidazole 500mg IV every 8 hrs or
2. Ampicillin/sulbactam 3g IV every 6hrs plus doxycycline 100mg IV or PO every 12 hours or
3. Ciprofloxacin 200mg IV every 12 hrs plus doxycycline 100mg IV or PO every 12 hrs plus metronidazole 500mg IV every 8hrs

Oral Treatment:

Regimen A:

1. Ofloxacin 400mg PO twice a day for 14 days plus
2. Metronidazole 500mg PO twice a day for 14 days

Regimen B:

1. Ceftriaxone 250mg IM once or
2. Cefoxitin 2g IM plus probenecid 1 g PO in a single dose once or other Parenteral third generation cephalosporin e.g., ceftizoxime, cefotaxime Plus doxycycline 100mg PO twice a day for 14 days

Follow Up:

For outpatients follow up should include examination, screening for C.trachomatis and N. gonorrhea

Sex Partners:

Examine and treat if they have had sexual contact during the 60 days preceding the symptoms

Pregnancy:

Hospitalized and treated with IV antibiotics.

HIV Infection:

Higher rates of concomitant Candida and HPV infections and HPV related cytologic abnormalities. Immunosuppressed HIV infected women should be managed aggressively using one the parenteral regimens.

Epidydimitis:

Recommended regimens:

For epidydimitis most likely due to gonococcus or chylamdial infection :

1. Ceftriaxone 250 mg IM in a single dose plus doxycycline 100mg PO twice a day for 10 days. For epidydimitis most likely caused by enteric organisms, or for patients allergic to cephalosporins and / or tetracyclines :
2. Ofloxacin 300mg PO twice a day for 10 days

Follow up:

Failure to improve within 3 days requires reevaluation of both the diagnosis and therapy

Sex partners:

Refer sex partners for treatment if contact was within 60 days preceding the treatment. Avoid intercourse until they and their sex partners are cured

HIV infection:

Same treatment regimens

Human Papillomavirus Infection :

External Genital Warts :

Recommended regimens :

Patient applied :

1. Podofilox 0.5% solution or gel , twice daily for 3 days followed by 4 days of no therapy. The cycle may be repeated for a total of 4 cycles, the total wart area should not exceed 10×2cm, and Podofilox should not exceed 0.5ml per day, its safety in pregnancy is not established or
2. Imiquimod 5% cream , three times a week for as long as 16 weeks, washed with mild soap 6-10 hrs later , its safety in pregnancy is not established.

Provider Adminstered:

1. Cryotherapy with liquid nitrogen or cryoprobe. Repeat every 1-2 weeks or
2. Podophyllin resin 10-25% in compound tincture of benzoin. Some experts recommend <0.5ml or < 1ocm2 per session, wash thoroughly in 1-4 hours, repeat weekly if necessary. Its safety in pregnancy not established or
3. Tricloro acetic acid or dicloro acetic acid (80-90%). Repeat weekly if necessary or Surgical removal either by tangential scissor excision, tangential , shave excision, curettage, or electrosurgery.

Alternative Treatments:

Intralesional Interferon or laser surgery

Cervical Warts:

For exophytic cervical warts exclude high grade squamous inta epithelial lesions and consult an expert for the management.

Vaginal Warts:

Recommended regimens:

Cryotherpy with liquid nitrogen or Tricloroacetic or bichloroacetic acid applied only to warts Repeat weekly if necessary OR Podophyllin 10-25% in compound tincture of benzoin applied to an area < 2cm2 per session. Repeat weekly. Its safety in pregnancy is not established.

Urethral meatus warts :

Recommended therapy :

1. Cryotherapy with liquid nitrogen or
2. Podophyllin 10-25% in compound tincture of benzoin, applied weekly if necessary, its safety in pregnancy is not established.

Anal Warts :

Recommended regimens :

1. Cryotherapy with liquid nitrogen or
2. Trichloroacetic or dicloro acetic acid 80-90 %, repeat weekly if necessary or
3. Surgical removal Management of warts on rectal mucosa left to an expert.

Oral Warts:

Recommended regimens:

1. Cryotherapy with liquid nitrogen or
2. Surgical removal

Follow-up:

For recurrences in first 3 months

Sex Partners:

Not necessary for the management of genital warts

Pregnancy:

Imiquimod, podophyllin, and podofilox should not be used, many advocate surgical removal. Cesarean section is not indicated to prevent transmission of HPV infection to the newborn.

Immunocompromised or HIV:

May not respond well, and may have frequent recurrences Squamous cell carcinomas might occur more frequently.

Squamous cell carcinoma in situ:

Patients with scams cell carcinoma in situ should be referred to an expert, ablative modalities effective, but careful follow up is important.

Subclinical Genital HPV Infection(without exophytic warts):

In the absence of co-existent dysplasia, treatment is not recommended.

Sex partners:

Examination of sex partners is unnecessary.

Vaccine Preventable STDs:

Hepatitis A:

Treatment:

Supportive, and avoid hepatotoxic medications

Prevention:

1. Good personal hygiene
2. Immune-globulin
3. Hepatitis A Vaccine- two dose series

Pre exposure prophylaxis:

1. Hepatitis A vaccine

Indications:

Homosexual men and Illegal drug users

Post exposure Prophylaxis:

Single IM dose of IG .02ml/kg up to 2 weeks after exposure

Hepatitis B:

Treatment:

1. Supportive and symtomatic care
2. Interferon -(40% effective in chronic hepatitis B
3. Antiretrovirals : Lamivudine is effective, others being studied

Prevention:

Vaccination, the following persons should receive it :

- Sexually active homosexual and bisexual men
- Sexually active homosexual and heterosexual men and women, including a) in whom another STD was recently diagnosed b) who had more than one sex partner in last 6 months c) who received treatment in STD clinic d) who are prostitutes
- Illegal drug users
- Health care workers
- Recipients of certain blood products
- Household and sexual contacts of people with chronic Hepatitis B
- People from countries where Hepatitis B is endemic
- Certain international travelers
- Clients and employees of facilities for the developmentally disabled
- Infants and Children and
- Hemodialysis patients

Vaccination schedule:

The most often used schedule is 0, 1-2, 4-6 months

Post exposure prophylaxis:

Exposure to persons who have acute hepatitis B:

Sexual contacts:

Should receive Hepatitis B Immune globulin and begin Hepatitis B vaccine series within 14 days of the sexual exposure.

Nonsexual household contacts:

Vaccination is encouraged especially children & adolescents, if HbsAg persists for >6mths all household contacts should be vaccinated.

Exposure to persons who have chronic HBV Infection:

Vaccination for both household and sexual contacts. Postvaccination serology indicated in sex partners and infants born to HbsAg positive women.

Pregnancy:

It is not a contraindication to hepatitis B vaccine or HbIG administration.

HIV Infection:

HBV infection more likely to lead to chronic HBV infection. Patients may need revaccination or may remain susceptible to HBV infection despite additional vaccine doses.

Proctitis, Proctocolitis, and Enteritis :

Recommended regimen:

1. Ceftriaxone 125mg IM plus doxycycline 100mg PO twice a day for 7 days

Follow Up:

Based on specific etiology

Sex partners:

Evaluated for any disease diagnosed in the patient.

Ectoparastic Infections:

Pediculosis pubis:

Recommended regimens:

1. Permethrin 1% crème to affected areas, washed in 10 mins or
2. Lindane 1 % for 4mins. Not recommended for pregnant or lactating women or children < 2yrs OR
3. Pyrethrins with piperonyl butoxide application for 10 mins. Pediculosis of eye treated with occlusive ophthalmic ointment twice a day for 10 days. Bedding and clothing should be decontaminated.

Follow up:

Reevaluated after 1 week, re-treatment if necessary should be with an alternative regimen.

Sex partners:

Partners within the preceding month should be treated.

Pregnancy:

Pregnant and lactating women should be treated with permethrin or pyretherins with piperonyl butoxide.

HIV Infection:

Same treatment regimen

Scabies:

Recommended regimen:

Permethrin cream 5% applied to all areas of the body neck down and washed off after 8-14 hrs.

Alternative regimens:

1. Lindane 1% lotion or 30gm cream neck down, washed in 8hrs or
2. Sulfur 6% ointment nightly for 3 nights. Bedding and clothing should be decontaminated.

Follow up:

If no response occurs within a week, retreat preferably with an alternative regimen.

Sex Partners and household contacts:

Both sexual and close household contacts within the preceding month should be evaluated & treated

Management of outbreaks in Communities and institutional settings:

Treat the entire population at risk and seek advice of an expert.

Infants, young children and pregnant or lactating women:

Should not be treated with Lindane, may be treated with Permetherin.

HIV Infection:

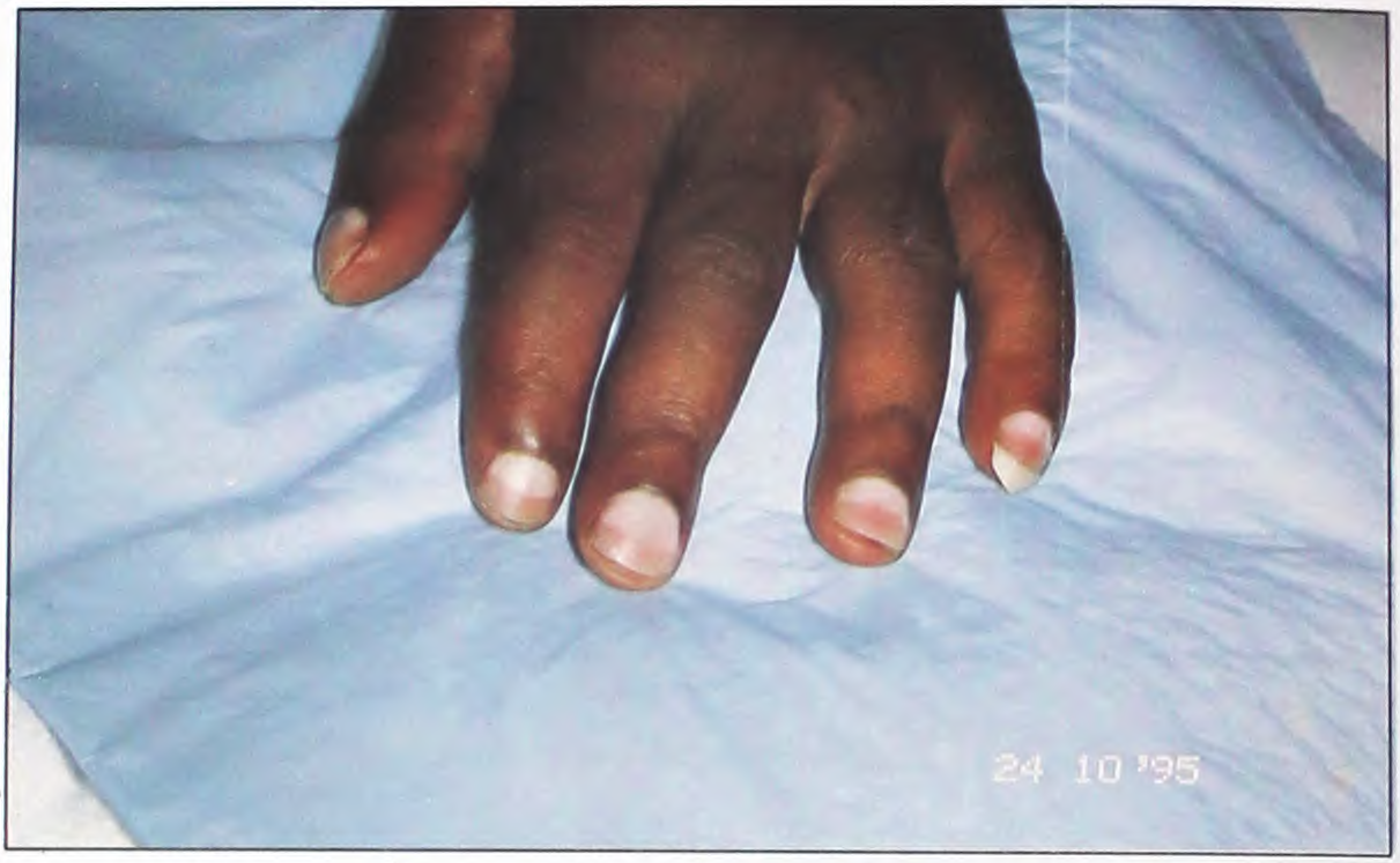
HIV patients and other immunosuppressed patients are at increased risk of Norwegian scabies, a disseminated dermatological infection; such patients should be managed in consultation with an expert, otherwise treatment regimens are the same

> *"I seek no sympathy .... the thorns which I have reaped one from the trees I planted; they have torn me and I bleed, I should have known what would spring from such a deed."*
>
> *Lord Byron*

(Courtesy Dr. Safdar, Principal, RIHFWTC, Srinagar)

Half and Half Nail Sign

Riyaz Bashir M.D., Faroque A. Khan MACP



A 35-year-old African American Male with terminal HIV disease and end stage renal failure on hemodialysis was admitted with a diagnosis of pneumonia and sepsis to our intensive care unit. The figue above depicts the classic "Half and Half nail" sign in this patient. According to Lindsay et al more than 95% of patients with this sign have renal disease. This sign is positive only when distal pink or brown zone is greater than 20% of the nail (Less than 20% would indicate white nails of Cirrhosis of Liver). There is no tendency of this pattern to grow out with nail hence this sign is produced by some unknown changes in the nail bed. The clinician should suspect some renal disease in patients who have this sign.

Address for Correspondence:

Faroque A.Khan, MACP
Chairman, Department of Medicine
Nassau County Medical Center
2201 Hempstead Tpke
East Meadow, NY 11554 (USA).

From Diary of a Verstile Teacher and Father Physician "Doctor Oslar"

Mohd Yousuf, MD; Kausar Yousuf, MBBS.

It is my long association with Medical students, who have been my life time-strength and inspiration, that I am making this effort to write about great "Doctor Oslar", with a hope that his message to medical students will strengthen their character and devotion to human service.

Dr. Oslar was a father physician, a humanist, motivator, an extra-ordinary clinician and great lover of students of medicine. As he says to the medical students on his first faculty appointment at the age of 25 with his overwhelming love for them.. "You come now into the society not of more professors," who would lecture at you from a distance but of men who are anxious for your welfare, who would sympathize with your difficulties and also bear with you weakness, look upon them as elder brothers to whom you could come confidently and fearlessly for advice in any trouble or difficulty.

Dr.Charles S. Byran in his book on William Osler makes an attempt to analyse and consolidate his message for doctors and students of medicine as under:-

1. Time management
2. Career Planning
3. Mentoring
4. Positive thinking
5. Education augmented by a bed side Library.
6. Caring for Patients
7. Communicating with patients
8. Seeking a balanced life.

Oslar attributed his success not only to hardwork or career planning but also to rich network of interpersonal relationship he had developed. He recognized that what makes or breaks our luck is a quality our bond with our fellow humans, he sought older people who would offer knowledge and insight and soughing young also i.e. students of medicine that could magnify his effectiveness and ensure his legacy. He said practical wisdom can't be learnt from books. A mentor can teach you this. His regard for mentor can be known from the fact that he dedicated his books on medicine not to parents or relatives but to his mentors.

Oslar loved having, hero's both living or dead as a source of inspiration for medical students. He said that from the books of these great Hero's, we get sutle influences which gives knowledge.

Oslar gave students access to his time and library. By the age of 47 he had began the custom of spending saturday evening in the company of medical students. He would invite students by turns and spend an hour or so with them. He would give them a piece of advice from favourite readings of great authors of medicine or literature.

Oslar, would take tremendous interest in showing medical students his old medical books. This was the enthusiasm and warmth of this versatile motivator. Enjoying the cultural show at a young age was no match to him than company of medical students. He would teach medical students about desire to know truth, sleadfastness and open and honest heart free of suspicion and jealousy. He asked students to show gratitude to their teachers. He says "I have exceptional happiness in the profession of my choice and I owe all this to my teachers and friends "I have sought success in life and I got it in the company and friendship of the members of my profession. He goes to say, I never departed from my ambition to be first of all the servent of my brethoren willing and anxious to do anything, within my power to help them. He further advised students let each days work not absorb your entire energies and satisfy your wide ambition. The students who are worrying about their future, too anxious over examination, are certain not to do well.

Oslar's advised that being methodical and thorough may make a great medical student but he says your character will still lack that what gives permance to power i.e. the grace of humility. It was great Oslar himself who had both self esteem and humility. He said, I have learned to be a better student and to be ready to say to my fellow students "I do not know this." He says that the secret of successful working lies in systamatic arrangement of working and its methodical performance and so make out a time table with the hours of lecture, studying and recreation and follow it closely. I know of no better way to accomplish a large amount of work and it saves the mental worry and anxiety which will surely haunt you if you tables are done in an irregular way.

Let us resolve to take the message of Dr. Oslar to become better doctors with devotion, discipline self esteem and above all being humanistic in our approach.

Prof. M. Yousuf
GMC. Srinagar.
Courtesy - Dr. Riyaz Bashir (USA)
who suggested me to read about Dr Oslar's greatness

Suggested Reading:
Osler Inspirations from a Great Physician (Ed.) Charles S.Bryan.
Oxford University Press, Oxford.

Natural History of Diabetic Ketoacidosis - SKIMS Apporach

A retrospective hospital based study in Endocrine services of Shen-Kashmir Institute of Medical Sciences, Srinagar, Kashmir. The records of 1294 diabetic patients comprising of 167 type I diabetics mellitus, 1087 type II diabetes and 40 fibrocalculous pancreatic diabetes patients admitted over the last 8 years were studied for diabetic ketoacidosis.

Thirty six causes of diabetic ketoacidosis were seen. The study group included 20 males and 16 females. Twenty seven were known diabetics while 9 (25%) presented with diabetic ketoacidosis as their first clinical manifestation. The major recognised precipitating factors were infection (78%) and omission of insulin (14%). In this series mortality was 33%. The major risk factors which contributed to mortality were delayed hospitalization, older age, severe acidosis and severe peripheral vascular insufficiency.

Diabetic ketoacidosis occurred most often in patients with known diabetes, with infection and cessation of insulin therapy as main precipitating factors. Mortality was significantly higher whcih could be reduced by improving patients-education, early hospitalization and aecess to care.

Source: Zargar AH; Sofi FA; Masoodi SR; Clinical biochemical and therapeutic aspects of diabetic ketoacidosis and its outcome. Saudi Medical Journal 1998; Vol. 19(4): 446-52.

Unusual presentation of Idiopathic Hyperprolactinemia

In this report we describe a 37 year old lady who was demonstrated to have hyperprolactinemia causing amenorrhea-galactorrhea syndrome. Computerized tomography scan done twice did not reveal and sellar or suprasellar abnormality and there was no clinical or biochemical evidence of primary hypothyroidism. She had regression of galactoorrhea, resumed regular menstrual cycles, and conceived twice on bromocriptine therapy. Following her second delivery she noticed spontaneous remission of galactorrhea and, prolactin levels estimated multiple times were normal.

Source: Zargar AH; Wani AI; Laway BA. Spontaneous remission in idiopathic hyperprolactinemia. JAPI 1998; Vol. 46: 485-87.

Gradual reduction of enalapril dosage after disease regression caused no worsening of symptoms or function

Evidence has grown over the last few years that prolonged antihypertensive treatment can achieve not only a reduction in blood pressure (BP) but also regression of cardio-vascular remodelling-particularly with regard to structural and functional alterations of small arteries. Cardiologists from Spain had reported that after prolonged administration of enalapril in hypertensives, the BP was maintained at normal values, left ventricular (LV) mass was reduced and function was on the results seen after the dosage of enlaparil was progressivelyf reduced after 7 years of treatment.

28 patients with essential hypertension who took 20 mg enalapril 12 hourly for 5 years were studied. At that time, the treatment was interrupted for 8 weeks after which it was resumed with the 12 hourly dose progressively increased from 2.5 to 20 mg. At the 7-year checkup, all the patients had normal BP. The 12 hourly dose was then reduced 15 mg for 3 months, 10 mg for the next three months and to 5 mg for the next three months unless the diastolic BP was over 90 mm Hg or systolic BP over 140 mm Hg, when a higher dose was returned to.

Four patients were withdrawn from the study due to side effect and uncontrolled hypertension. The authors found that only 5 patients did not have both normal diastolic and normal systolic BP. They say that this encourages the hope that maintenance of the cardiovascular alterations and not personal characteristics. The results also encourage hopes that low dosages of enalapril may achieve the same improvement in prognosis for patients with

Oral ciprofloxacin seems appropriate in children when indicated

Although offically still contraindicated, quinolones are used ever increasingly in paediatrics. Arthropathy has not been observed even with the most sensitive detection methods in children (mostly with cystic fibrosis) where it has been used. Doctors from Finland and Germany, using a new formulation, investigated the single-dose and steady-state pharmacokinetics of ciprofloxacin suspension and its metabolities in children not suffering from cystic ifbrosis (CF).

16 non-CF patients from 0.3 to 7.1 years were given the new suspension formulation of ciprofloxacin (10 mg/kg body weight) orally three times daily. The researchers observed that the drug was rapidlky asbsorbed. The maximum plasma concentrations with the mean varying from 1.7 to 3.6 mg/L were reached within 1 hour almost regardless of whether single dose administration or steady state. they found that the mean oral clearance ws lower in children < 6 years of age than those ≥ 6 years. The terminal half-life values with the means varyhing only between 4.2 and 5.1 suggest than dosing recommendations based on body weight are pertinent says the authors, although they advocate caution in small infants. They did not find any arthropathic or other adverse events atrributable to ciprofloxacin suspension.

The authors conclude that a dose of suspension form of ciprofloxacin of 10 mg/kig body weight given three times daily orally seems appropriate in children, provided the drug is clearly indicated.

Source: Heikki eltola, Pentti Ukkonen, Harri Saxen, Heino Stab. "Single-dose and steady-state phamacokinetics of a new oral suspension of ciprofloxacin in children"; Pediatrics; Vol. 101. No. 4, April 1998; pages 685-662.

Breech presentations at terrm is not a pre-requisite for caesarean section

This study comes from the Department of Obstetrics and Gynaecology. University of Geneva, Switzerland. The authors aimed to compared vaginal delivery versus elective caesarean for breech presentastion at term. Neonatal mortality and neonatal and maternal morbidity were al,so compared. The factors asociated with the risk of caesarean section during labour.

716 consecutive singleton breech births occurring at ≥ 36 completed weeks of pregnancy during the stuudy period. This represented 2.2% of all deliveries. 385 planned vaginal deliveries and 320 elective caesarean sections.

The major outcomes which were discussed were neonatal mortality and morbidity and maternal morbidity. Each of these entities had further parameters included withinthem to assess them further.

The auuthors defined maternal morbidity as endometrities, urinary infection, pulmonary infection, surgical complications, hysterectomy, anaemia, pulmonary emoblish, cardio-respiratory arrest. Planned vaginal deliveries had fewer maternal complications as compared to the elective caesarean section group. Five neonates with major maflormations died.

The authors defined neonatal morbidity as fracture, haematoma with hyperbilirubinemia, paresis, paralysis, visceral truma, respiratory distress, umbilical cord arterial pH<7.0 with 5 minute Apgar score <7. Both these groups did not show any variations as far as neonatal morbidity is concerned.

The study identified the risk factors as multiparity, martemal age more than 30 years and a higher body mass index. These factors were associated with a higher risk of intrapartum caesarean section.

These factors suggest that one cannot recommend elective caesarean section for breech presentation at term.

Source: Olivier Irion, Pascale Hirsbrunner ALmagbaly, Alfredo Morabia. "Planned vaginal delivery versus elective caesarean section: A study of 705 singleton term breech presentations"; British Journal of Obstetrics and Gynaecology; Vol. 105, July 1998; pages 710-717.

What is new in sexually transmitted diseases

Chris Carne, from the Department of Genitourinary Medicine, Addentbrooke's Hospital, Cambridge elaborates on the recent developments in sexually transmitted diseases. For this the author used Medline and recent journals.

The epidemiological changes which have occurred over the years are discussed. The author reports that even though gonorrhoea had been brought under adequate control in the UK, the resistant stains like penicilinase producing N. gonorrhoea and tetracycline resistant N. gonorrhoea required the switch of treatment to fluoroquinolones. The resistance to ciprofloxacin is also feared as also the combination of syphilis and HIV infection, says the author.

The diagnostic methods in current use include amplification assays like the ligase chain reaction which has an excellent scensitivity and specificity. The latest method of transcription mediated amplification which involves amplification of ribosomal RNA is alos useful. Antibody tests for herpes simplex type 2 are specific. Even the identification of asymptomatic carriers is possible according to the author.

The advances in the pharmacotherapeutic management include drugs against HIV. Triple therapy including a protease inhibitor along with two nucleoside analogue reverse transcriptase inhibitors is said to be better than dual therapy with two nucleoside analogue reverse transcriptase inhibitors. The new class of antiretroviral drug (non-nucleoside reverse transcriptase inhibitor - nevirapine) is effective.

Valaciclovir and famciclovir offer more convenient dosage regimens than aciclovir in herpes simplex infections. Chlamydia trachomatis can be treated with a single dose regimen of azithromcin.

As far as HIV infection is concerned, the author suggests the use of viral load tests (measures HIV RNA in serum) to predict the progression of disease. Typing of the human papilloma virus predicts the risk of progressive disease with the use dyskaryotic vaginal smears in high risk women.

Source: Chris Carne. "Sexually transmitted infections"; British Medical Journal; Vol. 317, 11 July, 1998; pages 129-132.

The International AIDS Society - USA Panel Antiretroviral therapy 1998 recommendations

An international panel of physicians with expertise in antiretroviral research and care of patients with HIV infection reviewed the available clinical and basic science study results. The data reviewed included phase 3 controlled trials, clinical, virologic and immunologic end point data, research conference data and HIV patho-physiology studies. The panel members opinions were also considered and the recommendations were made limited to the drugs available in mid 1998.

The antiretroviral therapy recommendations were made after updated recommendations were developed through consensus of the entire panel at each stage of development.

Although the accumulating data from various studies continue to support early institution of patent antiretroviral therapy in HIV infection, the panel says that the data is still incomplete on when precisely the therapy should be started. Since a variety of combination regimens show potency, there has been an expanding choice for initial regimens for individual patients. It has also been seen that plasma HIV RNA assays with increased sensitivity are important for monitoring therapeutic response but the precise levels of HIV RNA which defines treatment failure are yet to be determined. The panel has shown that long-term adverse drug effects are beginning to emerge which would require ongoing attention. The issues of optimal long-term approaches to antiretroviral management are yet unresolved.

The panel says that it will continue to monitor research findings in the field and provide updated recommendations are necessary.

Source: Charles C J Carpenter, Margaret A Fischi, Scott M Hammer, Martin S Hirsch, Donna M Jacobsen, David A Katzenstein, Jullo S.G. Montaner, Douglas D Richman, Michael S Saag, Robert T Schooley, Melanie A Thompson, Stefano Vella, Patrick G Yeni, Paul A Volberding. "Antiretroviral therapy for HIV infection in 1998-Updated recommendations of the international AIDS Society - USA Panel"; JAMA; Vol. 280, No. 1, July 1, 1998; pages 78-86.

Omeprazole does not carry a high risk of teratogenicity

In order to study the outcome of delivery after the maternal use of acid-suppressing drugs during early pregnancy. The authors conducted this study from Lund, Sweden, and a cohort of women identified by interview in early pregnancy were included in the study. The study was done since informationj about the use of omeprazole during pregnancy is very scarce.

A total of 547 women who were using acid-suppressing drugs with 553 infants. Six twin pairs were identified. All the infants that were exposed to acid-suppressing drugs were compared with all births in 1995-1996. The presence of congenital malformations were noted.

The authors found that the population of pregnant women using acid-suppressing durgs in early pregnancy is characterised by an increased maternal age, primigravida, increased rate of smoking during pregnancy.

The authors in this study paid special interest to omeprazole exposure since data on this drug were scarce. This study had a total of 282 omeprazole exposures. Among these exposures, nine infants with congenital malformations were identified (five cardiovascular defects, one Down's syndrome, two minor-facial anomaly and hypopadias). However, malformed foetuses diagnosed prenatally and aborted were not included.

The authors thus conclude that omeprazole carries no teratogenic risk. However, the possibility of the drug increasing the risk for very specific and rare malformations cannot be ruled out.

Source: Bengt Kallen. "Delivery outcome after the used of acid-suppressing drugs in early pregnancy with special reference to omeprazole"; British Journal of Obstetrics and Gynaecology; Vol. 105, August 1998, pages 877-881.

Laparoscopic cholecystectomy within 72 hours - preferred approach in acute cholecystitis

It is known that laparoscopic cholecystectomy for acute cholecystitis is associated with high complication and conversion rates although recent studies have shown it to be a safe and effective treatment. The optimal timing for the procedure remains unknown. The study from Hong Konga compared the safety and cost efficacy of early and delayed laparoscopic cholecystectomy for treatment of acute cholecystitis.

99 patients with a clinical diagnosis of acute cholecystitis were randomly assigned to early laparoscopic cholecystectomy within 72 hours of admission (49 patients, early group) or delayed interval surgery after initial medical treatment (50 patients, delayed group). The delayed group attack subsided after conservative management and elective laparoscopic cholecystectomy done 8 to 12 weeks later.

The results showed that 8 of the 41 patients in the delayed group underwent urgent operation at a median of 63 hours after admission due to spreading peritonitis (3 patients) and persistent fever (5 patients). It was seen that although the delayed group required less frequent modifications in operative technique and a shorter operative time, a higher conversion rate (23% vs 11%) and complication rate (29% vs 13%) was observed. In 38 patients who were admitted more than 72 hours of the onset of symptoms, the conversion rate remained high after delayed surgery (30% vs 17%). The authors also found that the delayed procedure was associated with a more prolonged hospital stay (11 days vs 6 days) and recuperation period (19 days vs 12 days).

The authors conclude that early operation within 72 hours of admission has both medical and socioeconomic benefits and is the dpreferred approach for patients managed by surgeons with adequate experience in laparoscopic cholecystectomy.

Source: Chung-Mau Lo, Chi-Leung Liu, Sheung-Tat Fa, Edward CS Lai, John Wong. "Prospective randomized study of early versus delayed laparoscopic cholecystectomy for acute cholecystitis"; Annals of Surgery; Vo. 227, No. 4, April 1998 pages 461-467. congestive heart failure as with high dosages say the authors. However, they advice awaiting the long-term study results before altering the routine maintenance of standard doses.

Source: Jose Ramon Gonzalez-Juanatey, Antonio Pose Reino, Jose Maria Garcia-Acuna, Alfonso Varela Roman, Carlos Calvo Gomez, Jose Cabezascerrato. "Effects on left ventricular mass and function of low doses of enlaparil for systemic hypertension"; The American Journal of Cardiology: Vol. 81, Jan. 1, 1998; pages 87-90.

With Best Compliments From:

CAULSON & CO

IST BRIDGE, SRINAGAR, KASHMIR; TEL. (O) 472145 (R) 474355

We Stock & Service
Littmann Stethoscopes

Authorised Dealers of:

Johnson & Johson Ltd.
Ethicon, Hospital Products & Ortho Divisions.

Birla 3M Ltd.

Stryker Products
(Div. of Nicholas Piramal India Ltd.)

Laparoscopic, Arthroscopic &
Sinuascopic Equipments.

Equipments for all Types of Orthopeadic,
Neurological & Spinal Surgeries

Editorial

NEW CLASSIFICATION OF DIABETES MELLITUS

In June 1987, American Diabetes Association (ADA) unveiled its new proposed criteria to classify and diagnose diabetes mellitus[1]. These recommendations culminated more than two years of collaboration amongst the experts from American Diabetes Association and the World Health Organization (WHO) thus replacing the earlier consensus documented produced in 1979 by the National Diabetes Data Group (NDDG)[2]. Some salient features of new classification include identifying four different types of diabetes: type 1, type 2, "other specific types" and gestational diabetes. Arabic numerals are specifically used thus avoiding any confusion of type II as the number 11. Insulin dependent (IDDM) and non-insulin dependent (NIDDM) terms are no longer encouraged to be used.

Type 1 diabetes (formerly called IDDM, type I, or juvenile diabetes) is characterized by beta cell destruction mediated by autoimmune process. It usually develops before age 25 years in over 95 percent of patients. The insulin deficiency is absolute making insulin necessary for patient survival. It is associated with other autoimmune diseases. Antibodies against insulin and islet antigen glutamic acid decarboxylase (GAD) are present in serum of such patients. Their presence antedates onset of clinical disease making it possible to screen individuals at risk. In a small percentage of patients the evidence for autoimmune causation is lacking and hence the inclusion of term "idiopathic form" of type 1 diabetes.

Type 2 diabetes (formerly called type II, maturity onset or adult onset diabetes) is characterized by peripheral insulin resistance and a gradually progressive beta cell secretory failure. It is the most prevalent form and highly associated with family history.

The definition for diagnosis of gestational diabetes was left unaltered. Remaining types of diabetes with known aetiologies were bundled together as "other specific types" including genetic defects in insulin action or beta cell function, drug or chemical induced, genetic syndromes associated with diabetes, and endocrinopathies.

The new diagnostic criteria for diabetes now include a definition of normal fasting plasma glucose being 110 mgs/dl or less. Fasting plasma glucose of 126 mgs/dl or more is considered diagnostic of diabetes (fasting implying a minimum 8 hour fast). Plasma glucose levels between 111-125 mgs/dl identify a new category destignated as IFG or impaired fasting glucose. By glucose tolerance test, a 2 hr plasma glucose of 200 mgs/dl or more after a 75 gram glucose load continues to remain diagnostic as well.

The new fasting glucose cut off was chosen since it predicts outcome such as retinopathy as well as the 2 hour post prandial level of 200 mgs/dl. This was based on data from the National Health and Nurtitional Epidemiology Survey (NHANES III)[3]. Because of lack of uniformity in standards for testing glycosylated hemoglobin, it was not chosen as a diagnostic test. It might be stated that many have argued in favour of glycosylated hemoglobin being used as a diagnostic tool since it correlates strongly with several adverse outcomes[4,5].

The impact of new diagnostic criteria will be enormous. First it will unmask those patients with type 2 diabetes who were previously labeled 'normal', and contributed significantly to the pool of diabetic patients who remained undiagnosed (it was assumed that 50% of patients with type 2 diabetes are not aware of their disease). In the United States, close to 2 million patients will be now identified from this pool.

While new diagnostic criteria are very likely to serve the intended purpose in western hemisphere, it is unclear as to what relevance they will have in eastern hemisphere where epidemiological normative data are largely lacking. It is time perhaps to undertake studies that will try to establish whether or not new proposed cut offs are clinically relevant. Using them without establishing a sound basis for doing so would only increase the burden of care without tangible proof that disease indeed exists. It is very true that new ideas must be embraced and adopted, but each idea must have a context. Without establishing a context, physicians in Indian subcontinent would be doing a disservice, and not advancing science. Even in countries like the United States, there is a faint murmur of dissent seeking to establish fair rationale and uncovering the evidence[6].

Romesh Khardori, MB., MD., FACP.
Professor-Director, Division of Endocrinology, Metabolism & Molecular Medicine, Department of Internal Medicine, Southern Illinois University School of Medicine
701 N. First Street, P.O. Box 19636, Springfield, IL 62794-9636
U.S.A.

JK-Practitioner 1999; 6(2):96.

References:

1. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997;20:1183-1197.
2. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. National Diabetes Data Group. Diabetes 1979;28:1039-1057.
3. Harris MI, Flegal KM, Cowie CC et al. Prevalence of diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey 1988-1994. Diabetes Care 1998; 21:518-524.
4. McCance DR, Hanson RL, Charles MA et al. Which test for diagnosing diabetes? Diabetes Care 1995;18:1042-1044.
5. Davidson MB, Peters AL, Schringer DL. An alternative approach to the diagnosis of diabetes with a review of literature. Diabetes Care 1995; 18:1065-1071.
6. Woolf SH, Rothemich SF. Editorial: New Diabetes Guidelines. A closer look at evidence. Amer Fam Phys, 1998; 58:1287-1290.

IRRITABLE BOWEL SYNDROME AND GUT MOTILITY (AN OVERVIEW)

G.N.Mir, B.Sc., M.Pharm, MBA, Ph.D.

Irritable bowel syndrome (IBS) is one of the most common and perplexing disorders in gastroenterology. The etiology of IBS is unknown and the absence of organic disease makes the diagnosis of IBS to be one of the exclusion. IBS affects primarily adults and is characterized by marked alterations in gut functions, (e.g. bowel habits) which are usually accompanied by pain. Although conflicting views exist, the basic underlying pathophysiological abnormality of IBS is thought to be a disorder of intestinal motility. This article deals with the anatomical, physiological, hormonal, therapeutic and drug development aspects of IBS and specifically its relationship to gut motility.

Anatomical overview of Motility

In IBS the major focus of inquiry is the intestines. The duodenum is the widest and shortest segment (10-12 inches) of the gut and is followed by the longest segment (5-10 meters) of jejunum and ileum. The first segment of the colon, the cecum begins at the ileocecal junction. The remainder of the colon is composed of the ascending, transverse, descending, sigmoid and rectal segments. The colon terminates at the anus.

There are four major anatomic layers that comprise the digestive tract. The outermost, the serosa, is composed of connective tisue and mesothelium. The longitudinal (outer) and circular (inner) muscle layers, composed of spindle shaped smooth cells, constitute the next layer, the muscularis externa. In the large intestine, the longitudinal muscle layer is grouped into three thick muscular bands called taenia coli. The layer adjacent to the muscle layers is the submucosa which contains connective, lymphatic and vascular tissue. Finally, the innermost layer, the mucosa, is marked by an epithelium which permits absorption and secretion, neurovascular tissue and endocrine cells. The neural input to the gut has dual origins, extrinsic and intrinsic. The extrinsic neuronal fibers originate from the vagal, pelvic and mesenteric nerves. These extrinsic neuronal fibers comprise the visceral efferent and visceral afferent nerves that enter and exit the gut through autonomic nerve plexuses associated with blood vessels. The vagus supplies efferent parasympathetic innervation to the stomach, small intestine and proximal colon. The pelvic and hypogastric nerves supply the colon with parasympathetic and sympathetic efferents, respectively. The mesenteric nerve branches from the celiac, superior and inferior mesenteric ganglia supply sympathetic innervation to the stomach, and the small and large intestines.

The intrinsic innervation of the gut is coordinated by a plexus of nerve fibers and constitutes the enteric nervous system of the gut. This local nervous mechanism which controls gut motility was first observed by Bayliss and Starling (Gershon and Erde, 1981). The plexus of nerve fibers present in the submucosa is called Meissner's plexus (or submucosal plexus). These postganglionic fibers of sympathetic origin are derived chiefly from the superior mesenteric plexus and are mostly nonmyelinated. The plexus of nerve fibers that are located in between the circular and longitudinal layers of muscle in the muscularis externa is called Auerbach's plexus (or myenteric plexus). The preganglionic fibers of parasympathetic origin comprise this plexus and are derived from the vagus nerve. These fibers synapse with he cells of the terminal ganglia in the plexus which corresponds to the parasympathetic ganglion cells.

One of the neurotransmitters involved in gut functions acetylcholine (ACh) is released from the preganglionic vagal and sacral fibers to the gut. The major action of ACh is on motility. The postganglionic fibers that provide sympathetic innervation to the gut, release the catecholamine, norepinephrine (NE). It appears that 5-HT acts as a neuron to neuron communicator, and affects both smooth muscle and the enteric neurons to cause: 1). activation of neurons that release ACh and are excitatory on longitudinal and circular muscle, 2) activation of nonadrenergic and noncholinergic intrinsic inhibitory neurons.

In 1970, it was suggested by Baumgarten (Gershon & Erde, 1981) that the enteric nervous system contains peptidergic neurons. One of these peptides is vasoactive intestinal peptide (VIP) which is found in large amounts in the intestine (Said and Mutt 1970). VIP-

JK-Practitioner 1999; 6(2):97-100

From Drug Research Laboratories, Inc. Bulkingham, USA (Mir)
Received December 1998 Accepted March 1998
Correspondence to : G.N.Mir, President & CEO Drug Research Laboratories, Inc. P.O.Box No 394, Buckingham, PA-18912, USA

immunoreactive neurons are present in the myenteric and submucosal plexuses with the axons directed in an oral to anal direction. These myenteric-CIP neurons appear to terminate both within the circular layer of smooth muscle and the neurons of the myenteric plexus. The action of VIP are to relax the gut and to increase the firing rate of many neurons in the myenteric plexus. The function and characteristics of the other peptides (i.e., somatostatin, substance P and the enkelphalins) require further study.

Physiological Overview of Motility

The physiological aspects of gut motility center on two basic properties: 1) electrophysiological events and 2) contractile events. The electrical events leading to the contraction of muscle cells arise from changes in membrane potential. The presence of constant fluctuations in the potential is called the basic electrical rhythm (BER) or slow waves. The frequency of the slow waves varies at different segments of the gastrointestinal tract, yet are constant regardless of the contractile state of the muscle. A second component of the myoelectrical pattern is the spike potential which is the electrical event that initiates the contraction of smooth muscle (Christensen, 1975, Bortoff, 1976, Tucker and Schuuster, 1982). The presence of the BER connotes that an underlying myogenic factor controls these myoelectrical events. The second component of motility regulation are neural factors. The application of cholinergic agonists such as methacholine, carbachol and physostigmine increased the duration of slow waves and spike activity but had no effect on the frequency of slow waves. These responses were inhibited by anticholinergic agents indicating that cholinergic agents mediate their effects by acting upon muscarinic receptors. The effects of adrenergic agents such as epinephrine or norepinephrine were biphasic. At low concentrations these agents were stimulatory (increase incidence of spike potentials) while higher concentrations yielded inhibition of spike activity.

This biphasic effect was upon the adrenergic alpha-receptors, since activation of adrenergic beta-receptors resulted in inhibition. The duration of slow waves was increased by serotonin, which also increased spike potential activity. This response is inhibited by methysergide, indicating that serotonin acts directly on smooth muscle. Therefore, along with the myogenic factors, neural factors appear to influence and regulate changes in motility.

Since the myoelectrical activity reflects changes in motility, it has been investigated to identify the possible relationship between altered slow wave activity and colonic motor dysfunction in IBS patients vs. normal patients. In the colon, the BER reveals two frequencies, six and three cycles per minute. In IBS patients, the three cycle per minute frequency was increased or occupied a greater percentage of the total BER vs. normal.

Hormones and Motility

The polypeptide hormones such as secretin, cholecystokinin, gastrin, motilin, glucagon and vasoactive polypeptide are among the gut hormones that have been widely investigated for their effects on the gastrointestinal motility. The effects of cholecystokinin on gut motility are similar to those of gastrin. Colon smooth muscle myoelectrical activity was shown to increase (via increase in spike potentials) when exposed to cholecystokinin, but required a higher concentration than gastrin (Snape, 1979). The alterations of spike potentials and motor activity were shown to increase in the colon (Dinoso 1973, Snape,1978), small intestine (Gutierrez, 1974, Dollinger, 1975, Castresana, 1978) and stomach (Castresana, 1978) when gastrin or cholecystokinin was infused. The administration of cholecystokinin or gastrin also yielded increase in colonic motor activity which was associated with the occurrence of abdominal pain (Harvey & Read, 1973). This indicates the possible roleof cholecystokinin in the changes in motility and abdominal pain following the ingestion of a meal. Finally, as with gastrin, cholecystokinin also causes the doubling of acetylcholine output in longitudinal ileum muscle (Vizi, 1973). Yet cholecystokinin's effect is mediated directly on smooth muscle (Bitar 1979, Snape 1982) and requires extracellular calcium to cause alteration in the myoelectrical pattern (Snape 1982). Another hormone which increases motility is motilin. The bolus infusion of motilin stimulated spike potentials in the antrum and duodenum and this response was more potent than with cholecystokinin (Castresana, 1978). The influence of secretin on intestinal motility is inhibitory by itself or by the opposing the actions of cholecystokinin. The infusion of secretin directly inhibits the cholecystokinin-induced increases in the myoelectrical activity in the colon (Dinoso, 1973), the small intestine (Gutierrez, 1974, Dollinger 1975) and the antrum of the stomach (Castresana 1978). The inhibition of motor activity can also be caused by glucagon. This effect occurs directly on colonic smooth muscle and is effective against food or morphine-induced motor activity in the colon (Chowdhury and Lorber, 1977).

Therapy

There is no cure or therapeutic modality that has been established that significantly alters the course of IBS.

Therefore, the goal of the physician is to implement some therapeutic regimen to control and minimize the symptoms of IBS. The effectiveness of several classes of agents such as antidepressants, spasmolytics (or anticholinergics), calcium-channel blockers and alpha$_2$ adenoreceptor agonist have been investigated in the attempt to relieve the symptoms associated with IBS. Overall, each has exhibited modest efficacy in relieving the symptoms associated with IBS, but the usefulness of these agents has not been established (Table 1).

Table-1: Medications that affect G1 Motility and Transit Tests

Anticholinergics
Tricyclic antidepressants
Narcotic analgesics
Calcium channel blockers (acutely, not chronically)
Adrenergic agents (alpha$_2$ adenoreceptor agonist)

Tricyclic antidepressants mechanistically suppress the central nervous system through: 1) potentiation of the actions of biogenic amines (i.e., norepinephrine) in the CNS by blocking the reuptake at adrenergic nerve terminals, 2) antagonism of muscarinic cholinergic and alpha-adrenergic response which results in the side effects.

Another class of drugs is the spasmolytics, also called anticholinergics. These agents act upon the muscarine receptors via competitive antagonism of acetylcholine, thus preventing muscle contraction, which decreases the tone and motility of the gut. The usefulness of the anticholinergic agents in IBS is doubtful because of the side effects and because a placebo was as effective in a patient study (Ivey, 1975). Calcium-channel blockers and alpha$_2$ adenoreceptor agonist inhibit the movement of calcium ions into muscle cells resulting in the inhibition of the excitation-contraction coupling events. The potential application of calcium-channel blockers and alpha$_2$ adenoreceptor agonist as smooth-muscle relaxants in IBS was presented in a favourable, but cautious review by (Traube and McCallum, 1984) (Digoseph and Mir, 84,86), (Taylor and Mir, 82).

Drug Development and Motility

A wide variety of techniques have been employed to measure the effect of drugs on motility. To describe in detail each preclinical and clinical test system is beyond the scope of this article. A brief list of the techniques and general description will be presented.

Preclinical test models:

Gastric emptying of liquid or solid meal in rodents, dogs and primates.

Transit time studies in rodents, dogs, primates using non-labeled or radio-labeled markers.

Chronic implantation of electrodes or strain-gauge tranducers on antrum, duodenum, ileum and colon in dogs or primates to record migrating motor complexes.

Fecal output studies in rodents.

Isloated tissue studies to study the mechanism of drug action.

Clinical models:

Time-lapse radiography, liquid barium, fluoroscopy with radiopaque markers Pressure-sensing telemetry capsules, water-filled manometry catheters, pressure sensing balloons and strain gauges for the measurement of intraluminal pressures.Sigmoidoscopic observation of orally administered transit markers.Since there are advantages and disadvantages to each technique with certain limitations on obtainable information, some techniques have been used in combination. The direct observation of movement in the gut can be studied using liquid barium fluoroscopy with radiopaque markers. Finally, there is the myoelectrical recording which only reflects the pattern of contractions via changes in the smooth muscle membrane potential. (Camilleri et al 98).

The value of the above techniques have given some insight into the patterns of gut smooth muscle contractions and the movement of luminal contents. One pattern of contraction is segmentation which involves the contraction of isolated segments of circular smooth muscle. In the small intestine, two types of segmentation occur: 1) eccentric contractions which involve short segments (les than 2 cm) and do not empty the segment's contents and do not change the intraluminal pressure, and 2) concentric contractions which empty longer segments (greater than 2 cm) and do increase luminal pressu[illegible]

Th[illegible] contractions are nonpropulsive and can mo[illegible]l contents in either direction from the point of contracture, but the net effect is to move chyme in the aboral direction. Another type of contraction is peristalsis, which is a progressive wave of contraction of successive rings of circular muscle moving down the small or large intestine. Finally, mass movements occur which propel luminal contents distally over long distances and are usually involved in the process of defecation.

The observation of myoelectrical pattern indicates patterns of individual contractions, but the observation of these patterns over longer periods of time (e.g., hours) reveal the presence of a cyclic activity. The earliest description of this cyclic activity was in 1911 by Boldyreff (see Weisbrodt 1981), noting that gastric contractions occurred every eighty minutes in the intestines of fasted dogs. It wasn't until fifty-two years later that Jacoby (Jacoby 1963) observed that the pattern in fasted dogs was cyclic and differed from fed dogs. These cyclic activities were initially termed the interdigestive myoelectrical complex, but since these patterns were observed in other species (i.e., sheep) to occur during feeding, it is now known as the Migrating Motility Complex (MMC). There are four types of contractile activity that are observed. A basal pattern where no contractions occur is followed by a preburst phase which shows an increase in contraction number and amplitude. Then, the burst or spike potential occurs where contractions are evident and then ends, returning to the basal pattern. The fourth pattern is an intermediate pattern of random contractions of varying amplitudes. This pattern is observed in a recently fed animal.

Conclusion

Gastrointestinal (GI) motility sutdies were initially directed towards an understanding of physiology and pathophysiology, but in recent years, these studies have been found to be clinically helpful in evaluating patients with suspected disorders of GI motility, particularly IBS. The focus of this article has been to examine mechanisms of various forces controlling GI motility and their impact on IBS and new means to combine these varying forces for sorely needed new and innovative drug development.

References:

1. Bitar K N. "Interaction of acetylcholine and cholecystokinin with dispersed smooth muscle cells." Am J physiol 1979; 237(2): E172.
2. Bortoff, A. Myogenic control of intestinal motility. Physiological Reviews, 1976; 56: 418.
3. Camilleri, M., Hasler, WL. and Parkman H.P. "Measurement of Gastrointestinal Motility in the GI Laboratory." Quigley Em. and Soffer, E, Gastroenterology; 1998; 115: 747-762.
4. Castresana, M. "Effects of motilin and octapeptide of cholecystokinin on antral and duodenal myoelectrical activity in the interdigestive state and during inhibition by secretin and gastric inhibitory polypeptide". Digestion 1978; 17: 300.
5. Chowdhury A. and Lorber S H. "Effects of glucagon and secretin on food-on morphine-induced motor activity of the distal colon, rectum and anal sphincter". Digestive Diseases and Sciences. 1977; 22(9): 775.
6. Christensen, M; "Myoelectrical control of the colon." Gastroenterology 1975; 68: 601.
7. DiJoseph, J F. Taylor, J A. and Mir, G.Nabi. "Alpha$_2$-adrenoceptors in the gastrointestinal system-A new therapeutic approach." Life Sciences, 1984; 35: 1031-1042.
8. DiJoseph, JF. and Mir, G. Nabi. "Lidamidine's effects on the lower gastrointestinal tract": A Review. Drug Develop. Res: 1986; 7(2): 101-109.
9. Dinoso, V.P. "Motor responses of the sigmoid colon and rectum to exogenous cholecystokinin and secretin". Gastroenterology 1973; 65: 438.
10. Dollinger HC. "Effects of secretin and cholecystokinin on motor activity of human jejunum". Digetion 1975; 12: 9.
11. Gershon, MD and Erde, SM. "The nervous system of the gut". Gastroenterologyly 1981; 80(6): 1571.
12. Gutierrez, JG, Chey, WY, and Dinoso, V.P. "Actions of cholecystokinin and secretin on the motor activity of the small intestine." Gastroenterology 1974; 67: 35.
13. Harvey, RF and Read, AE. "Effect of cholecystokinin on colonic motility and sympatoms in the patients with the irritable bowel syndrome". Lancet 1973; 1: 7793.
14. Ivey KJ. "Are antichloinergics of use in the irritable colon syndrome"? Gastroenterology 1975; 68: 1300.
15. Jacoby, HI, Bass P and Bennett DR. "In vivo extraluminal contractile force transducer for the gastrointestinal muscle". J. Apyl Physiol 1963; 18: 658.
16. Said, SI and Mutt, V. "Polypeptide with broad biological activity. Isolation from small intestine". Science 1970; 169: 1217.
17. Snape, W J, Matarazzo, S A, and Choen, S. "Effect of eating and gastrointestinal hormones on human colonic myoelectrical and motor activity." Gastroenterology 1978; 75: 373.
18. Snape, W J, and Cohen S. "Effect of bethanecol, gastrin I or cholecystokinin on myoelectrical activity". AM J Physiol, 1979; 236(4): E 458.
19. Snape W J. "Effect of calcium on neurohormonal stimulation of feline colonic smooth muscle". AM J Physiol 1982; 243: G134.
20. Taylor, J.A. and Mir, G. Nabi. "Alpha Receptors and Gastric Function: Current Trends Review". Drug Develop. Res: 1982; 2(2): 105-122.
21. Traube M and McCallum R W. Calcium-channel blockers and the gastrointestinal tract. AM J Gastroenterology. 1984; 79(11): 892.
22. Tucker, H and Schuster, M.M. "Irritable bowel syndrome: Newer pathophysiologic concepts". Adv. Intrn. Med. 1982; 27: 183.
23. Vizi, S.E. "Evidence that actylcholine released by gastrin and related polypeptides contributes to their effect on gastrointestinal motility." Gastroenterology 1973; 64: 268.
24. Weisbrodt, N.W. "Motility of the small intestine". In Johnson, L F (ed) in Physiology of the Gastroenterology Tract. New York, Raven Press 1981.

LATEST RADIOIMAGING TECHNIQUES FOR DIAGNOSING PORTAL HYPERTENSION; A REVIEW ARTICLE WITH SPECIAL EMPHASIS ON SONOGRAPHIC FINDINGS

Basharat Hussain Shah M.D.; Tanveer Mir M.D. FACP.

Effective methods for diagnosis of portal hypertension and demonstration of portosystemic collaterals include ultrasonography, barium studies, endoscopy, arterial and transhepatic portography. However, ultrasonography is an initial, reliable, noninvasive technique which can detect portal hypertension even before its clinical manifestations. Modern gray-scale ultrasonography can very well delineate minute details of portal circulation, assess the patency of portal vein, distinguish presinusoidal blocks from intrahepatic and postsinusoidal blocks besides demonstrating varices and collateral pathways.

Portal hypertension refers to an increase in portal venous pressure more than 12 mm Hg (normal 5-10 mmHg). This pressure is difficult to measure and consequently the term is used as a syndrome characterised by splenomegaly and portosystemic venous anastomosis. Real time sonography is an initial noninvasive screening method. The demonstration of vascular networks in portal hypertension is greatly facilitated by the use of this technique which allows rapid imaging in any possible plane. The main portal vein is best and most readily visualized in right anterior oblique position in relation to the sound beam with 15-40 of obliquity. Measurement of portal vein is obtained at its broadest point just distal to the union of splenic and superior mesentric vein. There is no difference between the portal vein measurements of male and female patients. The ultrasonographic findings in the caliber of the portal venous channels in portal hypertension were first reported by Weinreb and Kumari etal[1]. The demonstration of patency of the umbilical vein, which normally is obliterated at birth has been stressed as a specific finding for portal hypertension[2]. This recanalization provides portosystemic communication from left portal vein to superficial epigastric veins. The two factors commonly measured during sonography include the caliber of the portal vein at the largest point directly in front of inferior vena cava and the caliber variation in normal and pathological portal vein during phases of respiration. The portal vein diameter greater than 13mm (normal: 11-12mm) is a fairly characteristic sign of portal hypertension. However in some cases with haemodynamically effective portosystemic shunt the portal vein size may remain small. Further in some cases failure of visualization of portal vein at portahepatis coincides with complete occlusion of portal vein as in direct invasion of the portal vein by tumor mass. In such cases solid echogenic shadow are seen within the lumen of the portal vein[3,4]. Lack of normal caliber variation (an increase during inspirtion and decrease during expiration) in one of the major tributaries of portal vein during breathing provides another sonographic evidence of portal hypertension[5]. The sensitivity and specificity of this sign is 79.7% and 100% respectively, in comparision to portal vein dilatation sign where sensitivity is only 41.8%[5].

The other sonographic signs described in literature such as the comma shaped appearence of the portal trunk, the accumulation of the perporital echoes, the slight dilatation of splenic and superior mesentric vein radicles in an enlarged spleen should be considered non specific signs of portal hypertension. The demonstration of portosystemic shunts such as esophagogastric varices and splenorenal shunts are additional sonographic findings. These collaterals appear as anechoic channels sonographically. Aneurysmal dilatation of portal vein, although unusal, can be considered another sonographic evidence of portal hypertension. The assessment of portal venous system using splenic venography percutaneous portography and other invasive procedures provide better images than sonography but are associated with inherent risks of mortality and morbidity. This is so because patients suffering from portal hypertension often have impaired coagulation or renal function compounding the risks inherent in any invasive study. Also in such patients splenoportography and angiography fail to display the portal vein due to diversion of contrast material into large

JK-Practitioner 1999; 6(2): 101-103

From the Department of Internal Medicine Nassau County Medical Center (Shah, Mir)

Received December 1998 Accepted March 1999

Correspondence: Dr. Tanveer Mir MD, FACP Associate Program Director Nassau County Medical Center State University of New York at Stony-Brook 2201 Hempsted Turnpike, East Meadow New York 11554, USA.

portosystemic venous collaterals. Hence such invasive procedures are unacceptable as screening test. Only selected patients with liver cirrhosis and suspected portal hypertension are studied angiographically usually when a therapeutic surgical procedure is contemplated. In cases of acute gastrointestinal haemorrhage an enlarged portal vein on ultrasound could rapidly identify portal hypertension as a possible etiology. Sonographic portography can be used to screen adolescents and adult patients with cystic fibrosis for the onset and progress of portal hypertension. In such cases it was possible to identify portal hypertension before it was clinically manifested by measuring the caliber of portal vein.

Dupplex doppler examination is another reliable tool in investigation of portal vein patency and flow direction is largely based on the quantitative estimation of flow velocity and volumetric rate in the portal vein. This examination can be performed on patients of any age without sedation and can establish the diagnosis of clinically portal hypertension. Technical success rate of this method of 95%[6]. Inversion of the normal orthograde hepatopetal flow in superor mesentric vein on doppler examination imply presence of mesentric-caval shunt via renal or gonadal veins. Reversed flow in splenic vein along with enlarged renal vein imply splenorenal shunt.

Angiography is another invasive procedure and remains the gold standard for evaluating the status of portal vein and hepatic venous systems. It can determine vascular pressure but cannot assess blood flow rate. Percutaneous transhepatic portography delineates portal venous system and is the best way of showing collateral vessels. Direct splenoportography has major advantage in that portal pressure can be measured directly. In arterial portography contrast material is injected into coelic axis and superior mesentric artery for adequate visualization of vascular bed. Major disadvantages of this method is inability to measure portal pressure and inadequate delineation of portal venous systems in low venous states. Hepatic venography, used mainly to diagnosis Budd Chiari Syndrome, is helpful in cases of intrahepatic portal obstruction. On hepatic venography portal vessels appear sparse, distorted and unevenly distributed producing winter tree appearance. Invasive procedures for the measurement of portal pressure or blood flow are applied for scientific and pharmacological queries only (Frank et al).

Magnetic resonance imaging of liver using gadolinium shows reduced portal blood flow in patients with cirrhosis and portal hypertension. Mean peak enhancement value of hepatic parenchyma after intravenous gadolinium is significantly altered in such patients[12]. Time to peak enhancemet is also significantly delayed. Measurement of portal blood flow by phase contrast MRI is helpful in predicting intrahepatic or extrahepatic shunting and is of value in detecting progression of stages in diffuse liver dissease[13]. In summary, of all the tests available sonography is a simple, non-invasive procedure capable of diagnosing portal hypertension. Besides, duplex sonography the combination of real time and pulsed doppler sonography can highly make this technique even more useful for such a purpose. Colour Doppler flow imaging (CDFI) represents an extension of duplex sonography as it makes velocity information available not only for a small region but also for a large segment or even for the whole image. CDFI is an important alternative to angiographic methods in the diagnosis of vascular disturbances in the portal system. In addition selectie patients may benefit from MRI and other invasive techniques.

References:

1. Weinerb Jeffery, Kumari Shiela, Philips Gail, Pochaczevsky Rubem: Portalvein measurements by real time sonography: AJR, Sept. 1982; 139: 497-499.
2. Weill F: Ultrasonographic visualization of an umbilical vein. Radiology. Jul. 1976; 120: 159-160.
3. Okuda K, Musha H, Yoshida T, et al; Demonstration of growing casts of hepatocellular carcinoma in portal vein by celiac angiography- The thread and streak sign. Radiology 1975; 117: 303-309.
4. Webb LJ, Barger LA, Sherlock S: Greyscale ultrasonography of portal vein, Lancet 1977; 2: 675-677.
5. Bolondi Luigi, Gandolfi-Lionello, Arientil Vincezo, Caletti Giancarlo, Corcioni Eugenio, asbarrini Giovanni, Labo Giuseppe: Ultrasonography in diagnosis of portal hypertension. Diminished response of portal vessels to respiration: Radiology Jan. 1982; 142: 167-172.
6. Patriquin Heidi, Lafortune Michael, Burnspeter N, Dauzat M: Duplex doppler examination in portal hypertension: Technique and anatomy AJR July 1987; 149: 71-76.
7. Kane A. Robert Katz Shuart G. The spectrum of sonographic findings in portal hypertension: A subject review and new observations. Radiology Feb. 1982; 142: 453-458.
8. Glazer M. Gary Laing C. Faye, Brown W Thomas, Gooding A.W. Gretchen: Sonographic demonstration of portal hypertension: The patent umbilical vein. Radiology July 1980; 136: 161-163.
9. Jutner Hans-Udo, Jenney M. Joanne, Ralls Philips W, Goldstein Leonard I, Reynolds B. Tefler: Ultrasound demonstration of portosystemic collaterals in cirrhosis and portal hypertension Radiology Feb. 1982; 142; 459-463.
10. Tamada Takashi, Moriyasu Fuminori, Onos, Shimizu K, Sohy, Kawasaki T, Kimura T, Yamashita Y, Someda H, Hamato N, U Cnino H. Portal blood flow with MRI. Radiology 1989; 172: 639-644.
11. Nelson C: Random comparision of pulsed doppler sonography and angiography in patients with portal hypertension. AJR July 1987; 149: 77-81.
12. Soyer P. Dufresne AC. Somveiu. A: MR imaging of the liver

Effect of portal hypertensionon hepatic parenchymal enhancemet using a gadoloinium chelate: Joumal of Magnetic Resonance imaging 1997; 7(11): 142-6.

13. Kashitani N. Kimoto S. Tsunoda M, Ito T, Ono A, Hiraki Y: Portal blood flow in the presence or absence of diffuse liver disease: measurement by phase contrast MR imaging. Abdominal imaging 1995; 20(3): 197-200.
14. Subramanyam BR, Balshazar EJ, Modamba MR, Raghvendra BN, Hornii Sc. Lefleur RS: Sonography of POrtosystemic venous collaterals in portal hypetension. Radiology 1983; 146:161-66.
15. Kumari S, Weinreb J, Pochaczevsky R, Philips L, G. Ross, Gorvoy J: Real time sonographic evaluation of the portal vein in patients with cystic fibrosis; Scientific exibit at the annaul meeting of the Radiological Society of North America, Chicago Nov. 1981.
16. Shabel SI, Rittenberg GM, Javid LH, Cunningham J. Ross P.: The bull eye falciform ligament: A sonographic findig of portal hypertension. Radiology 1980; 136: 157-59.
17. Haag K.: Current diagnosis of liver diaseases: Duplex ultrasonography. Schweiz Rundsch MEd Prax. 19 Nov.1996; 85(47): 1524-8.
18. Frank B Zoller WG: Diagnosis and therapy of Portal Hypertension; Leber Magen Darm. Nov. 1996; 26(6): 284-90, 293-7.
19. Uno A. Ishida H. Konno K. Ohnami Y. Naganuma H. Niizawa M. Hamashima Y. Masamune Portal hypertension in children and young adults: sonographic and color Doppler findings Abdominal imaging: Jan-Feb. 1997; 22(1): 72-8.
20. Ahn J. Copper JM. Sillberzweig JE. Mitty HA. Venographic appearence of portosystemic collateral pathways. British Journal of Radiology Dec. 1997; 70(840): 1302-6.

JK-Practitioner

Get a

Free Copy

for your library

Make sure new ideas and information flow freely to your colleagues and students.

Complete and return the Library Recommendation Form printed below, and we will send you a complimentary copy of **JK-Practitioner** for your institutional library.

To: Collections Development Librarian	**From:**
Name of Library ____________	Your name ____________
Name of Institution ____________	Street address ____________
Street address ____________	City, State, Code ____________
City, State, Code ____________	

HIV – THE CURRENT AND FUTURE EPIDEMIC: AN OVERVIEW

Gurpeet Singh, M.D.; Musarat Shareeff, M.D; Majid A. Khan, M.D; Robert H. Clark, M.D.;Tanveer Mir, M.D.; Faroque A. Khan, M.B., M.A.C.P.

HIV - The Current and Future Epidemic:

The HIV-AIDS pandemic that started in the early 80's has claimed some 11.7 million lives globally according to the World Health Organization (WHO) UNAIDS estimates. Currently 30 million people are infected/harbouring the HIV virus – two-thirds of whom live in sub-Saharan Africa. It is estimated that in 1997, 5.8 million people (including children) were infected with HIV, representing roughly 16,000 new cases daily, more than 50% of whom are the young adults aged 15-24.

WHO points out that although 50% of reported AIDS cases are in developed countries, more than 90% of all estimated cases of AIDS are in developing countries. The USA has reported a decline in AIDS-related deaths in the past two years. In developed countries, the average survival time after a diagnosis of AIDS has increased from less than one year to between one and three years; whereas, the survival time after a diagnosis of AIDS in developing countries is less than six months.

HIV/AIDS in Asia:

Asia, which inhabits about 60% of the world's population, is experiencing an explosive HIV/AIDS epidemic with devastating consequences to its public health. By the turn of the century, most new HIV infections in the world will probably occur in Asia. India has among 3-5 million people who are HIV infected, the largest estimated number of HIV-infected adults in the world. Unlike western countries, the spread of HIV in India is by heterosexual transmission, fueled by both married and unmarried men visiting prostitutes. Roughly 30-60% of female prostitutes in metropolitan cities in India are estimated to be HIV infected. Professional blood donors, migrant workers, and truck drivers are also responsible for spread of the disease.

Surveillance:

The principal method involves conducting surveys to determine the prevalence of HIV by testing anonymous blood samples (sero-surveys). These sero-surveys are done among specific groups or cohorts of individuals over a period of time to monitor changes in prevalence.

The Virus:

HIV is one of a group of viruses known as retroviruses. It is icosahedral in shape, and consists of a central core containing RNA, along with an enzyme-reverse transcriptase This enzyme is responsible for converting its RNA into DNA. This change in genetic machinery due to reverse transcriptase is responsible for the dreaded pathogenicity of the HIV virus. There are two main types of HIV viruses - HIV-1 and HIV-2. They cause the same spectrum of disease, but HIV-2 does so more slowly. HIV-1 is the dominant type in the whole world, except for sub-Saharan Africa where HIV-2 predominates.

Pathogenesis:

Once HIV enters into a host cell, it releases its RNA and the enzyme-reverse transcriptase. The enzyme-reverse transcriptase uses the viral RNA as a template to form a DNA copy, which is then integrated into the host cell's own DNA. Hence, the host cell ceases to carry out its function and becomes a virus factory. HIV infects multiple systems, and many different cells in the human body, including brain, lymph node, lung, bone marrow, thymus gland, and skin. The monocytes and macrophages become reservoirs of infection. However, HIV has a particular affinity for CD_4 cells or T4 helper cells. According to extensive research, duration of infection and viral replication is concentrated in CD_4 cells. Hence, infection with HIV ultimately leads to a decrease in the number of CD_4 cells in the body. The depletion of CD_4 cells is one of the most conspicuous signs of HIV infection. CD_4 count is often used as a measure of disease progression, or of the response to

JK-Practitioner 1999; 6(2): 104-107

From Nassau County Medical Centre, East Meadow, NY (Gurpreet, Musarat, Khan, Clark, Mir, Prof. Faroque)

Received December 1998 Accepted February 1999

Correspondence: Gurpreet Singh, M.D., Department: of Medicine, Nassau County Medical Center, 2201 Hempstead Turnpike
East Meadow, NY 11554

treatment. Early viral isolation from the blood can be done at the time of initial infection (before the immune response is established, and/or in advanced disease when the immune system is overwhelmed. Antibody response to HIV is unable to eradicate or completely suppress the infection, unlike other viral infections. With the onset of AIDS, the level of anti-p24 antibodies decrease and the level of p24 increases - this serological finding is consistent with the tremendous virus load and suppressed antibody response. HIV disease progression appears to be affected by age, sex, general health, and mode of infection. A number of identifiable stages are associated in the progression of infection.

Asymptomatic Phase:

Seroconversion occurs 2-12 weeks after initial infection and is often accompanied by a flu-like illness. During this clinically latent phase, the virus is actually very active and appears to be continuously replicating in the lymphoid tissue. Up to 10 billion new copies of virus are produced each day. These new viruses enter and destroy CD_4 cells. Most HIV-infected CD_4 cells have an average life span of two days.

However, a pool of latently and chronically infected cells continues to exist. These cells produce low levels of virus continuqusly, or may enter a dormant state from which they may be reactivated at a later stage. Initially, however, new immune cells match immune-cell destruction. Eventually, viral replication exceeds that of new CD_4 cell production.

Symptomatic Phase:

At some stage individuals start experiencing the first symptoms of disease. This manifests typically as enlargement of the lymph nodes in the neck, armpits, or groin. The progressive destruction of immune system results in severe and persistent illnesses. Without treatment, the average time from the initial infection to the development of AIDS is around 10-12 years in young adults. This is, however, faster in children and older people. This development of AIDS from initial infection can be extended by early therapy. A healthy immune system has around 600-1200 CD_4 cells/mm^3; whereas, due to profound destruction of the immune system in advanced stages of AIDS, individuals may have fewer CD_4 cells/mm^3. The fewer the CD_4 cell count, the more will be the complications. Table 2 shows the correlation between CD_4 cell count and complications that can occur in patients with AIDS. A small number of infected people, 5-7 percent, remain healthy despite more than 12-15 years of HIV infection. These individuals, termed as "long-term non- progressors, are possibly infected with genetically less pathogenic strains of HIV.

Table 1
AIDS Surveillance Case Definition for Adolescents and Adults : 1993

CD_4 Cell Categories	A Asymptomatic; PGL; Acute HIV Infection	B Symptomatic (not A or C)	C AIDS Indicator Condition (1987)
> 500/cu mm (> 29%)	A1	B1	C1
200-499/cu mm (14 – 28%)	A2	B2	C2
< 200/cu mm (< 14%)	A3	B3	C3

Classification of individuals with HIV Infections

A number of ways have been used to classify people

Table 2
Correlation of complications with CD_4 Cell Counts

CD_4 Cell Count	Infections	Non-Infections
> 500/mm^3	Acute retroviral syndrome; Candidal vaginitis	Persistent generalized lymphadenopathy (PGL); Guillain-Barre syndrome; Myopathy; Aseptic meningitis
200-500/mm^3 Neoplasia	Pneumococcal and other bacterial pneumonia; Pulmonary TB; Herpes Zoster; Thrush; Candidal esophagitis; Cryptosporidiosis; Kaposi's sarcoma; Oral hairy leukoplakia	Cervical intraepithelial cancer; β-cell lymphoma; Anemia; Motoneuronal multiplex; Idiopathic thrombocytopenic purpura; Hodgkin's lymphoma; Lymphocytic interstitial pneumonitis
< 200/mm^3	P. carinii pneumonia; Dis. chronic Herpes simplex; Toxoplasmosis; Cryptococcosis, Disseminated histoplasmosis and coccidiodomycosis; Cryptosporidiosis; Chronic microsporidiosis, Miliary/extrapulmonary TB; Progressive multifocal leukoencephalopathy (PML); Candidal esophagitis	Wasting; Peripheral neuropathy; HIV-associated dementia; CNS lymphoma; Cardiomyopathy; Vacuolar myelopathy; Progressive polyradiculopathy; Immunoblastic lymphoma
< 50/mm^3	Disseminated CMV; Disseminated M. avium complex	

with HIV infection. The popular one developed by the Center for Disease Control and Prevention (CDC) in the United States of America is widely in use. The CDC classification system for adolescents (> 13 years of age) and adults divides the consequences of HIV infection into categories on the basis of CD_4 cell count and illnesses associated with HIV (Table 1). Patients in A3, B3, and C1 - C3 are reported as AIDS, based on the AIDS-indicator conditions or a CD_4 cell count $<200/mm^3$. Pulmonary TB, invasive cervical cancer, and recurrent pneumonia are three new additions to the AIDS indicator condition (Table 3). Symptomatic conditions that a) reflect a defect in cell-mediated immunity, or b) whose clinical course is complicated by HIV infection; e.g., peripheral neuropathy, PID, ITP, listeriosis, diahhorea of more than one month, cervical dysplasia, thrush, vulvovaginal candidiasis, etc., are not included in Category C.

TABLE 3

Conditions in Case Definitions of AIDS (Adults) - 1995

- Candidiasis, of esophagus, trachea, bronchi or lungs - 5,422 (11%)
- Cervical cancer, invasive - 166 (0.3%)
- Coccidioidomycosis, extrapulmonary - 140 (0.3%)
- Cryptococcosis, extrapulmonary - 1,626 (4%)
- Cryptosporidiosis with diarrhoea > 1 month - 760 (1.6%)
- Cytomegalovirus of any organ other than liver, spleen, or lymph nodes; eye 3,105 (6%)
- Herpes simplex with mucocutaneous ulcer > 1 month, or bronchitis, pneumonitis, esophagitis - 1,927 (4%)
- Histoplasmosis, extrapulmonary - 309 (0.7%)
- HIV-associated dementia : Disabling cognitive and/or other dysfunction interfering with occupation or activities of daily living - 1,872 (4%)
- HIV- associated wasting : Involuntary weight loss > 10% of baseline plus chronic diarrhoea (> 2 loose stools/day > 30 days), or chronic weakness and documented enigmatic fever > 30 days - 6,618 (14%)
- Isoporosis with diarrhoea > 1 month - 39 (0.1%)
- Kaposi's sarcoma in patient under 60 years (or over 60 years) - 2,729 (6%)
- Lymphoma, non-Hodgkin's of β-cell or unknown immunologic phenotype and histology showing small, noncleaved lymphoma or immunoblastic sarcoma - 1,039 (2.2%)
- *Mycobacterium avium*, disseminated - 2,042 (4%)
- *Mycobacterium tuberculosis*, disseminated - or pulmonary - 2,214 (5%)
- Nocardiosis
- *Pneumocystis carinii* pneumonia - 13,096 (28%)
- Pneumonia, recurrent-bacterial (> 2 episodes in 12 months) - 1,829 (4%)
- Progressive multifocal leukoencephalopathy - 327 (0.7%)
- *Salmonella* septicemia (non-typhoid), recurrent - 78 (0.2%)
- Strongyloidosis, extraintestinal
- Toxoplasmosis of internal organ - 1,550 (3%)
- Wasting syndrome due to HIV (as defined above - HIV-associated wasting)

Laboratory Diagnosis

The standard test is ELISA serology for antibody detection. ELISA screening assay and a conforming western blot on ELISA immunoassay-positive specimens is the most common assay. Also, detection of virus with p24 antigen or growth in culture establishes the presence of HIV infection. There are two types: HIV-1 and HIV-2. HIV-1 is divided into sub-types 'A to I' and 'O'. ELISA screening tests maybe falsely negative before the seroconversion; i.e., 3 to 12 weeks after virus transmission, and it may miss the sub-type 'O'; hence, the assay may be repeated in high-risk groups in 3 to 6 months. On the other hand, western blot detects HIV-2 inconsistently and also fails to detect sub-type 'O'.

Recently, the FDA licensed ELISA Immunoassay (EIA) Diagnostic Test from Sanofi Diagnostic Pasteur Labs for use. This assay detects HIV-1 and HIV-2 with improved sensitivity and specificity.

Approaches to Treatment

Clinical advances against HIV continue at a very rapid pace. The aim of treatment is to reduce the number of HIV in the body, control its replication, and manage opportunistic infections. HIV/AIDS patients can benefit from treatment with medicines, but there is, as yet, no cure for HIV. The status of current drugs available to treat HIV infection, as per the guidelines provided by the U.S. Department of Health and Human Services, is as follows: 11 drugs are available - 5 nucleoside-reverse transcriptase inhibitors (NRTIs), 4 protease inhibitors, and 2 non-nucleoside-reverse transcriptase inhibitors (NNRTIs). By the end of 1998, two or more drugs will probably be added to this list.

Table 4

Drugs Currently Used to Treat HIV Infection

- Nucleoside analogues
    - Zidovudine
    - Didanosine
    - Zalcitabine
    - Lamivudine
    - Stavudine

- Protease inhibitors
    - Indinavir
    - Nelfinavir
    - Ritonavir
    - Saquinavir

- Non nucleoside reverse transcriptase inhibitors
    - Delavirdine
    - Nevirapine

- Drugs expected to be approved in 1998
    - Efavrinz (NNRTIs)
    - Abacivar (NRTIs)
    - Adofovir (a nucleotide)

Currently available drug options are targeted to inhibit one of two viral enzymes - reverse transcriptase or

Table 5

Recommendations from two Major Panels for the use of Antiretroviral Agents in HIV-Infected Adults

Subject of Recommendations	International AIDS Society	DHHS and Kaiser Family Foundation
When to Start Therapy	Acute HIV infection; symptomatic HIV infection; asymptomatic and CD_4 count < 500 c/mm^3, or viral load > 5,000-10,000 copies.	Acute HIV infection, symptomatic HIV infections; asymptomatic and CD_4 count < 500 c/mm^3, or viral load > 10,000 copies by branched-DNA assay, or > 20,000 copies by PCR.
What Drug To Start With	2 NRTIs plus a potent protease inhibitor.	2 NRTIs plus a protease inhibitor, or 1-2 NRTIs plus ritonavir and saquinavir.
	Alternatives: No. 1: 2 NRTIs and NNRTI 2 NRTIs plus Saquinavir No. 2: 2 protease inhibitors with or without 1-2 NRTIs	**Alternatives** No. 1: 2 NRTIs and NNRTI No. 2: NRTIs
When to Change Therapy	Preselected viral load ranging from < 50 to < 5,000. **Other Considerations:** CD_4 cell count, clinical complications.	Failure to eliminate detectable virus (< 500 copies/ml) **Other Considerations:** CD_4 cell count.

protease. Recently, identified 'Chemokine receptors' are envisaged as suitable targets for drug discovery, and research is now underway to explore their potential in treatment of HIV AIDS. Treatment with single antiretroviral agent leads to suboptimal virus suppression, and the rapid emergence of drug resistant virus. Such limitations have led to the current recommendation of treatment with a combination of antiretroviral drugs. Current practice shows that a combination of three or more drugs is needed to control the disease effectively. Triple therapy is currently the standard of care, which has resulted in reduction in viral load to undetectable levels in many patients.

Currently, a number of alternative approaches to anti-viral and immune therapy, like chemoreceptor blockade, antisense compounds, gene therapy, 'Trojan horse' viruses, passive immuno therapy, are under investigation. The inability of antiretrovirals to completely eliminate the virus and failure of antiretrovirals to reach 90% of the world's HIV-positive patients, the research for the development of therapeutic and protective vaccines should be pursued more vigorously.

References:

1. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. J. Kaiser Family Foundation. MMWR MORB MORTAL WKLY REP. 1998, 47(rr-5):#82.
2. Guidelines for use of antiretrovirals in HIV-infected adults and adolescents. Department of Health and Human Services and the Henry J. Kaiser Foundation. Ann Intern Med. 1998, 128(12 pt 2):1079-100.
3. JG Bartlett. Ann Intern Med 129(6).
4. AIDS: Images of the Epidemic. WHO, Geneva, 1994.
5. AIDS: The Third Wave. Editorial, Lancet 1994, 403.
6. HIV/AIDS Surveillance Report. Centers for Disease Control and Prevention (CDC), US Department of Health and Human Services, Division of HIV/AIDS, Atlanta, Georgia, USA, 30333.
7. Srikanth P, et al. Epidemiological features of acquired immunodeficiency syndrome in southern India. India Journal of Medical Research 1997, 105:191-197.
8. NIH Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents; 1997.
9. Carpenter CCJ, Fischl MA, Hammar SM, et al. Antiretroviral therapy for HIV infection in 1996. JAMA 1996, 276:146-154.
10. BHIVA Guidelines Coordinating Committee. British HIV association guidelines for antiretroviral treatment of HIV seropositive individuals. The Lancet 1997, 349:1086-1092.

PREVENTION OF SEPSIS IN NEONATAL INTENSIVE CARE UNIT (ICU)

Khursheed Sheikh M.S.; M Ayub Bhat M.B.B.S; Akash A Shah M.B.B.S.; Altaf Shera M.S. M.Ch; Rekha Patnaik M.S. M.Ch.

The sepsis is the leading cause of death in neonates admitted to the nurseries all over the world[1]. The magnitude and intensity of the problem is much more in the developing countries. While their march towards advancement and refinement of surgical technique, drug and nutritional therapy and other areas are appreciable, there is a lot of scope for improvement, preferably in prevention of sepsis[2,3]. Though the increasing use of antibiotics have altered the entire picture of neonatal infection, there are some aspects which are of surgical significance. Widespread systemic use of prophylactic antibiotic as a simple answer to an infective complication of a surgical procedure is fallacious. It is now recognized that most effective prophylaxis is the presence of high tissue concentration of antibiotic at the time of operation achieved by a single dose premedication[4]. Further postoperative antibiotic use is only confined to management of frank infection. Surgeons inspite of great care and attention face a high neonatal mortality due to sepsis in intensive care units (ICU)[3]. The mortality is more in intestinal surgeries performed for band obstruction, ileal atresia, necrotising enterocolitis etc.[2]. No infection in the new born is trivial[4]. The relative immaturity of the neonatal immune system is an important factor in the increased susceptibility to the infection[1]. The tendency to acquire infection in the hospital is enhanced as they are exposed to much more hostile flora in the early days of life and this increases the chance of sepsis in an operated neonate[5]. Strict attention to hand washing before handling a baby either directly or indirectly and thorough disinfection of his environment and supportive system will make us to achieve approximately 90-99% prevention of sepsis. This would leave only a negligible incidence which will keep us baffling and require further advancement for its total eradication.

To avoid the sepsis in the neonates operated for various lesions following measures for prevention of infection are recommended. They can be divided broadly into three groups.

1. Those related to the PERSONNEL (including babies relatives, doctors, nurses etc.).
2. Those related to the ENVIRONMENT, and
3. Those related to the NEONATE.

Some of these measures recommended may not be practical for all areas, due to financial and other restraints, however, they provide some idea for adaptation to practice.

PERSONNEL

1.Hand Washing: An effective hand washing is the single most important factor in the prevention of infection in neonatal units[1]. All people who will be touching the babies (parents, doctors, nurses and others) must wash their hands upto the elbow for at least two minutes. They must be sure that they have cleaned all the areas, including that between the fingers and under the finger nails, before touching them. If they handle more than one baby, they must wash their hands and forearms (again being sure to clean all areas) for at least 15 seconds before touching the next baby[1]. The ideal hand washing agent should kill or remove all pathogenic bacteria without irritating the skin, and should have persistent local action[6]. A number of studies have shown that transient microorganisms are removed almost entirely by washing with soap and running water, but the resident flora is difficult to remove with hand washing[2,3,5]. The ordinary hand washing releases bacteria into the air and therefore onto the surface in the nursery. Washing with surgical solutions containing either povidone-iodine, chlorhexidine-gluconate or hexachloroprophene prevents this release. Of the three, povidone-iodine is considered best because of its activity against the gram positive and gram negative organisms[1]. Great care must be taken to prevent the contamination of the agent used; otherwise it will itself act as source of the infection[2,4]. Bar soap must not be allowed to sit in a puddle of water. Dispensers of solution must be cleaned and rinsed thoroughly on daily basis and fluid container replaced[2,7]. Drying of the hands is best done with a hot air blower, but paper towel used only once or linen towels changed at least daily may be more practical[7,8]. Finally, a good hand washing

JK-Practitioner 1999; 6(2): 108-111

From the Department of Paediatric Surgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar (J&K), India.(Sheikh, Bhat, Shah, Shera, Patnaik)

Received October 1998 Accepted January 1999

Address for Correspondence: Dr. Khursheed Sheikh, Department of Paediatric Surgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar - 190 011, Kashmir, Post Bag No. 27, E-mail: root@skims.ren.nic.in

will be wasted if the tap is turned off by hand, or if the bin lid is lifted by hand to dispose off a paper towel. Foot operated taps and bin lids are the only reliable and effective ways of preventing recontamination[2].

2. Personnel Health: All personnel should be made aware that even a mild transmissible disease may prove fatal to a new born. Every one having contact with the baby should be encouraged to report any infection they harbour, to the staff incharge of nursery[3,7] and if transmissible they must not work in the nursery or the delivery area. Hospital policy should be such that staff having infectious illness are made to work in another area until their infection subsides, or they should be kept off, on paid sick leave[8]. Routine culturing of the personnel is not an effective way of preventing infection.

3. Attire: Caps and masks are not needed for routine care in the nursery. Masks, being effective for only a few minutes to few hours (depending on type) and may even be dangerous if wearer has false sense of security. However, long hair should be restrained and caps and masks (triple laminated and disposable) are advised for surgical procedures like insertion of umbilical catheters or chest drains[2]. Many writers advocate the wearing of a separate gown for each baby and if wet changing it daily or more frequently. Linen gowns if used are permeable to bacteria. Plastic aprons are cheaper than linen gowns, impermeable to bacteria and protect the areas most likely to be contaminated[6].

4. Staff Members: It is essential that there be an adequate number of staff, preferably one nurse for each baby, allowing her to wash hands in between. This allows for easier isolation, as one nurse cares one neonate only[6,7]. Similarly it is important to have supportive staff; such as cleaners; who are permanently assigned to the nursery to maintain high standard of technique.

5. Education: It is essential that all staff be provided with ongoing educational opportunities by courses or inservice lectures and seminars to upgrade their knowledge as this forms the corner stone of any preventive measure[8].

ENVIRONMENT

1. Design: The primary requirement is sufficient space for movement of people and bulky equipment around the cots without risk of touching next one. The American Academy of pediatrics recommended 80-100 square feet of space per patient, with at least 6 feet between incubators and 8 feet between aisles. There should be also adequate separate space for storage of linen, sterile supplies and equipment. There should be several conveniently placed wash-basins. The American Academy of Pediatrics recommended at least one per 6 infants or one per room in the smaller rooms[1]. Many microorganisms are capable of surviving in dust, so a minimum of dust collecting surface is advisable, and they should be damp-dusted daily to prevent the airborne contamination. Ways of minimizing dust collecting surface include the use of bench running along the wall with drawers in it (rather than shelves) for the storage of general items; and having things like oxygen, bottled air and suction piped in, to avoid having cylinders in the room. The isolation facilities may be useful for babies who are actively excreting large number of organisms, but the important factor is that they be cared by a separate staff member and a separate equipment[6]. The American Academy of Pediatrics also recommend adequate ventilation defined as, "providing a minimum of 12 changes of room air per hour ..... with air movement patterns that reduce drafts". However, many American nurseries can't meet this standard and there is no evidence to suggest any example of infection resulting from inadequate ventilation[1].

2. Protocol for Disinfection: To ensure that routine disinfection or sterilization is performed regularly and adequately, it is essential to have a written protocol devised and available to all staff members. This protocol should detail how and when each item or equipment is to be disinfected or sterilized. The protocol should be planned by consultation between the physician incharge of the nursery, the head nurse of the nursery, an expert on infectious diseases and a representative from the bacteriology laboratory. It is wise to have one person who is responsible for the operation of the protocol, and is logical that this person be a nurse[5]. In general, cleaning with a detergent to remove organic matter, followed by disinfection with appropriate agent, is satisfactory for equipments such as incubators, radiant warmers, monitoring equipment and for those items that do not penetrate the skin or airways, such as, stethoscopes and blood pressure cuffs[7]. Sterilization is obviously essential for all items which penetrate the skin or airway such as intravenous catheters, chest drains, endotracheal tubes and respiratory supportive circuits.

THE NEONATE

1. Skin Care: Preparations of hexachlorophene and chlorhexidine have been widely used as a skin wash to reduce the incidence of skin colonization. The hexachlorophene is mainly active against gram positive organisms and its use as a skin wash became widespread in the later 1950's as a part of an onslaught against staphylococcus aureus. Nurseries in Geelong (Australia) and Edinburgh (England) where accurate records were kept, noted that the incidence of both staphylococcal skin sepsis and colonization was already falling before hexachloroprophene bathing was introduced[6,7]. Ten years later, animal studies in the United States showed hexachloroprophene caused neurological abnormalities in rats and monkeys, and infants treated with it, showed detectable amounts of hexachloroprophene in their blood. This was most marked in the preterm infants who have especially permeable skin. Further study showed a spongio-form encephalopathy at postmortem in preterm infants and detectable levels of hexachloroprophene present in their brains. Because of this realization, its use as skin wash was stopped in 1970[1]. Chlorhexidine has a broad antibacterial action than hexachloroprophene. Although some forms have been noted to be absorbed, there is no documentation of any toxicity from skin washing. However, as the experience with the hexachloroprophene demonstrates, skin washing with antibacterial is not proven to reduce the incidence of skin colonization or infection, nor will it stop an outbreak of infection[6], it has been suggested therefore, that application of antibacterial substance to the skin is unnecessary as long as proper hygienic standards are maintained[1].

2. Umbilical Cord Care: The umbilicus has been treated with an even greater variety of substances than the skin to reduce the colonization. In addition to hexachloroprophene and chlorhexidine, the umbilicus has been treated with alcohol, polymixin, bacitracin and neomycin spray, silver sulphadiazine and with triple-dye. Iodine preparation are not suitable for this application because their repeated use on skin or umbilicus may result in their absorption and consequent interference with thyroid function[1,7]. Despite the widespread use of all the preparations mentioned here, there are not properly controlled trials to support their use. To the contrary a recent study indicated that such preparations can delay drying and separation of the cord when compared with removal of soiling with sterile water. But further studies are required to prove that the sterile water minimizes the colonization and hence the infection of the umbilicus[8].

3. Breast Feeding: Because breast milk is known to have anti infective properties through its transmission of antibodies. Although it invariably contains bacteria, breast milk is definitely safer than the artificial formulae when the quality of water cannot be guaranteed. Provided the mother has washed her hands thoroughly, and all equipment is sterile, bacteria found in breast milk will derive from the skin and ducts of the nipple[2,3]. These bacteria are probably important in establishing normal flora in the gastrointestinal tract of the infant, and the use of antibacterial substances on the nipples may be harmful by preventing this. For infants who cannot suck, expression and storage of the milk, to be used for gavage feeding is advisable. However, its use will only be safe if the equipments used for collection are sterile and it is used either immediately, or stored in a reliable refrigerator between 4 to 6°C (upto 72 hours). Pasteurization by heating to 62.5°C for 30 minutes has been advised for the breast milk[2,5]. While this process considerably reduces the number of live organisms in the milk, it will not destroy spores or some enterotoxins but will destroy many of its antimicrobial constituents and the lipase activity necessary for fat absorption.

4. Artificial Feeding: If safe storage or immediate use of the breast milk cannot be arranged, artificial milk feeds will be necessary. A separate area should be used ideally for washing and sterilizing bottles and utensils. If this is not possible, the bottles and utensils should be washed thoroughly to remove all the organic material, and then placed in the disinfectant, autoclave or water for boiling, and used thereafter. The hands must be washed thoroughly before removing bottles and utensils from the sterilizer and an aseptic technique maintained throughout the process[3].

5. Parenteral Nutrition: Where artificial feeding with the human milk or formula is not possible or is not sufficient, intravenous therapy will be necessary[3]. The dangers of infection with the umbilical and other central cannulae are well recognized, but it must be remembered that the peripheral intravenous cannulae also provide a ready access for microorganisms. Attention to the hand washing and site preparation when inserting and caring for a peripheral I.V line must be as strict as when inserting and caring for a central venous or arterial catheter[5]. Most infusion solutions will support the growth of the microorganisms, therefore aseptic technique must be used while giving them and the set changed every 48 hours along with the cannulae site. The set should be changed after every 24 hours, if fat emulsion or blood is given. The bacterial contamination of three-way taps has been reported, so it is preferable to add drugs to infusion fluids through the injection site on the container or tubing after first disinfecting it with 70% alcohol[2,5,8].

In summary, a careful attention to strict asepsis; as suggested; during the management or the handling of a neonate in the ICU will significantly reduce the sepsis, and hence the mortality.

References:

1. James L, Sutherland J, Tooley W: Standards and recommendations for hospital care of newborn infants. Am Acad Pediatr 1997, 23: 135-40.
2. Davies P, Gothefors L: Bacterial infections in fetus and newborn. Publish WB Saunders 1984, pp210-18.
3. Korones S: High risk newborn infants. Publish Mosby & O'Donnell Barry 1986, pp20-29.
4. Nixon Harold: Essentials of Paediatric surgery. Publish Butterworth Heinemann 1992, pp50-56.
5. Larson E: Rituals in infection control. Jr Obst Gynae & Neonatology Nursing 1987, 411-16.
6. Lowbery E, et al: Control of hospital infection: A practical handbook. Publish Chapman and Hall 1975, pp35-39.
7. Davies E, et al: An outbreak of infection with a methicillin resistant staphylococcus aureus in a special care baby unit. Jr Hospital Infec 1987, 10: 120-28.
8. Maurer L: Hospital hygiene. Publish Edward Arnold, 1978, pp140-46, 1978.

BM Scientific Company

GOLE MARKET, KARAN NAGAR, SRINAGAR - 10, KASHMIR

DISTRIBUTORS FOR:

- Borosil Glass Works Ltd., Bombay
- Gupta Scientific Industries, Amballa
- Elico Ltd., Hyderabad
- Loba Chemie Pvt. Ltd., Bombay
- Narang Scientific Works Pvt. Ltd., Delhi
- Sisco Research Laboratories Pvt. Ltd., Bombay
- Glaxo India Ltd., Bombay
- Whatman Ltd., UK
- S.D.Fine Chemicals, Bombay
- Ke-Roy Balances, Varanasi
- Dhona Instruments, Calcutta

A.F.P. SURVEILLANCE: A STRATEGY FOR POLIO ERADICATION

Basnır Gaash M.D.; Iftikhar H. Munshi M.D.; Basharat Nabi M.B.B.S.; Yasmeen Wani M.D.

Abstract: One of the main social goals of the countries all over the world is polio-eradication by the year 2000, and an effective surveillance is one of the pillars on which a successful eradication programme finally rests. Acute flaccid paralysis is the indicator for polio surveillance, and the WHO and Government (Central & State) are collaborating to spread the surveillance network across the length and breadth of the country. Our valley, where surveillance activities were started 1 year back, too, is proceeding towards an on-time elimination status.

Key words: Acute flaccid paralysis, Poliomyelitis, Surveillance.

JK-Practitioner 1999; 6(2): 112-115

In May 1998 the World Health Assembly resolved that the main goal for all the countries of the world should be eradication of poliomyelitis by the year 2000, which simply means no case of clinical poliomyelitis associated with wild poliovirus and no wild poliovirus found despite intensive efforts. To achieve this goal 4 complementary strategies were proposed, viz:

1. Achieving and maintaining highest coverage levels under the routine immunization programme.
2. Implementing National Immunization Days, popularly known as Pulse Polio Immunization (PPI).
3. Mop up rounds to wipe away the last lurking foci of wild poliovirus, and
4. Strengthening the surveillance of AFP so that all cases of polio are detected, reported and investigated in time.

Poliomyelitis has been eliminated from greater part of Europe and America, and presently southeast Asian regional countries happen to be the main foci of wild poliovirus. Globally there has been a 96% decline in reported cases of polio from 1987 to 1996[1]. This has been possible through mainly highest coverage in routine immunizations and also pulse polio programme. In India number of poliocases fell from 22570 in 1985 to 1005 in 1996[2]. Without doubt India is marching towards zero polio status, and as the number of polio cases decreases high quality surveilance assumes greater importance to detect and eliminate the remaining foci of polio transmission.

Elimination of polio from any country can be certified only when there are no reports of new cases of poliomyelitis caused by wild virus for 3 consecutive years inspite of adequate surveillance. Due to silent transmission and rapid spread of poliovirus the World Health Organisation considers a single confirmed case of paralytic polio as an outbreak[2].

Why AFP surveillance and not just polio surveillance:

Since paralytic polio is one of the causes of acute flaccid paralysis, maintaining a high degree sensitivity of AFP reporting will ensure that all cases of paralytic polio are detected, reported and investigated quickly. AFP surveillance, thus, is the international standard to assess the progress towards polio eradication and ensures that no case of paralytic polio is missed during the surveillance phase.

The World Health Organisation is collaborating with the Government of India in its drive for polio eradication. In this context the National Polio Surveillance Project (NSPS) was set up to monitor the progress in all the States and Union Territories of the country. In October 1997, the NSPS appointed 59 Surveillance Medical Officers (SMOs) to assist the State health machinery strengthen the surveillance network through the Directorate of Family Welfare, Maternal & Child Health, and Immunization.

What is meant by AFP:

Acute flaccid paralysis means a paralysis of acute onset (less than 4 week's) where the affected limb or limbs are flaccid (floppy or limp). Tone is diminished as evidenced by examination by palpation or passive movement of joints[3].

It is essential that suveillance is carried out for all

From the Department of Epidemiology, (Gaash) **National Polio Surveillance Project** (Munshi) **Department of Paediatrics Govt. Children Hospital** (Nabi) **and the Department of Community Medicine SKIMS, Soura** (Wani) **Srinagar Kashmir.**

Received December 1998 Accepted March 1999

Correspondence to : Dr. I.H.Munshi, SMO, Directorate of Family Welfare, MCH & Immunization, Old Secretariat, Sgr-1

Table - I. Differential Diagnosis of Paralytic Poliomyelitis

Signs and Symptoms	Polio	GBS	Transverse myelitis	Traumatic neuritis
Progression of paralysis	<4 days, maximum 7	From hours to 20 days	From hours to 40 days	From hours to 4 days
Fever onset	Present	Absent	Absent	Variable
Flaccidity	Acute, asymmetrical, proximal	Acute, symmetrical, distal	Acute, lower limbs, symmetrical	Acute, asymmetric limb
Muscle tone	Diminished	Diminished	Diminshed in lower limbs	Diminished in limb
DTRs	Decreased or absent	Absent	Absent in lower limbs	Decreased or absent
Sensation	Severe myalgia and back ache	Cramps, tingling, hypesthesia	Anesthesia of lower limbs	Pain in gluteal region
Cranial nerve	Only when bulbar and bulbospinal	Often present	Absent	Absent
Decreased respirations	Only when bulbar and bulbospinal	In severe cases	Absent	Absent
CSF: WBCs	High WBCs	< 10 WBCs	Normal	Normal
Protein	Normal or slightly Increased	High	Normal or slightly elevated	Normal
Bladder dysfunction	Transient retention	Sometimes	Present	Absent
Conduction velocity 3 wks	Normal, then slightly decreased	Abnormal, demylination	Normal	Abnormal in sciatic nerve
EMG - 3 wks	Abnormal	Normal	Normal	Normal
Sequelae	Severe, asymmetrical atrophy	Absent or minimal	Moderate atrophy	Peroneal atrophy

cases of AFP and not just poliomyelitis. Thus all AFP cases are required to be reported regardless of the final diagnosis. All cases below 15 years of age have now been included in the case definition (as against only under fives previously). It implies that any case of AFP, regardless of suspected cause and of any age, should be reported and investigated. This will ensure that no case of polio in the under 15 year age group is missed. It is worth noting that AFP in those aged more than 15 years of age is unlikely to be polio.

Experience in Europe and the America which have already eliminated polio from their region has indicated that a minimum of 1 case of AFP per 100,000 children below 15 years occurs in absence of polio. This is called the "Background rate" of the AFP among children and is due to other non-polio causes of acute flaccid paralysis. (Table 1)[4]. Such non-polio causes include Guillain Barre Syndrome (Infective polyneuritis), Transverse Myelitis, Traumatic Neuritis, Severe Hypokalaemia, Post-diphtheritic paralysis, Encepalitis, and botulism. The classification of AFP is temporary since within 10 weeks of the onset of paralysis the case should be reclassified as "confirmed" which means polio-induced AFP or "discarded" as non-polio. Table-II depicts the flow diagram of reclassification of AFP cases[5].

AFP Surveillance Methodology:

The various components of AFP surveillance methodology are:

1. Establishment of AFP reporting units in all districts:

All health institutions including hospitals, community health centres, and private nursing homes which are likely to see AFP cases are established as reporting sites. At least one individual (with one or two alternatives) is identified and made responsible for immediate reporting of AFP case to the Surveillance Medical Officer, Directorate of Family Welfare & MCH or the District Immunization Officer by the quickest possible means. The nodal person of the reporting unit should send timely weekly reports to the D.I.O. even if no AFP case was detected during that week (which is called the 'Nil' reporting). The reported cases need to be investigated by the SMO/DIO within 48 hours after notification.

Since the beginning of AFP surveillance activity 64 reporlting units have been established in all the districts of the valley including Leh & Kargil. The apical institutions (SMHS Hospital, SKIMS, Govt Childrens Hospital, Bone & Joint Hospital), district hospitals, sub-district hospitals, and Primary Health Centres have all been enlisted as reporting units.

2. Laboratory Investigations:

Two stool samples are collected 24-48 hours apart for each AFP case and shipped to the regional laboratory for virus isolation under strict reverse cold chain conditions (The designated lab for the J&K State is the Central Research Institute, Kasauli). Preferably the stool samples should be collected from the case within the first 14 days of onset of paralysis.

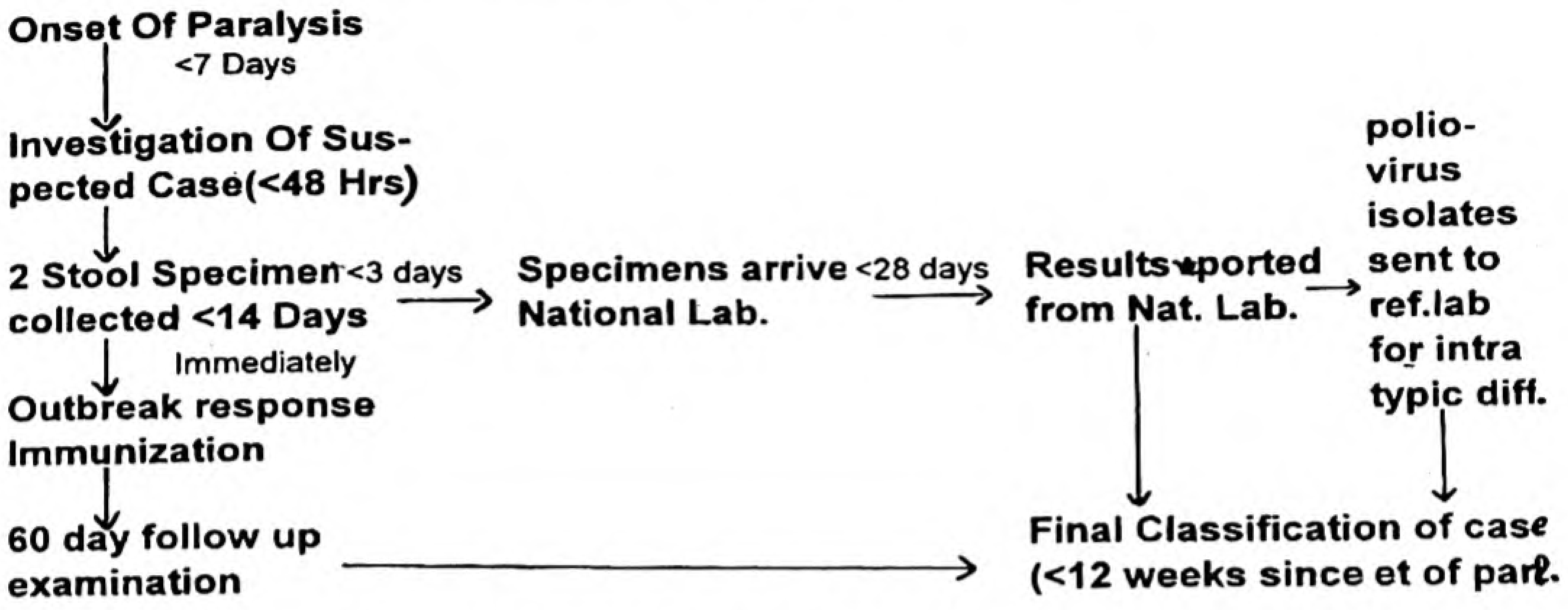
3. Active search & outbreak response immunization:

Active search has to be done by the DIO for detection of additional cases in the area from which an AFP case was reported, and if more cases are found they are investigated and their stool samples are also taken for laboratory investigation.

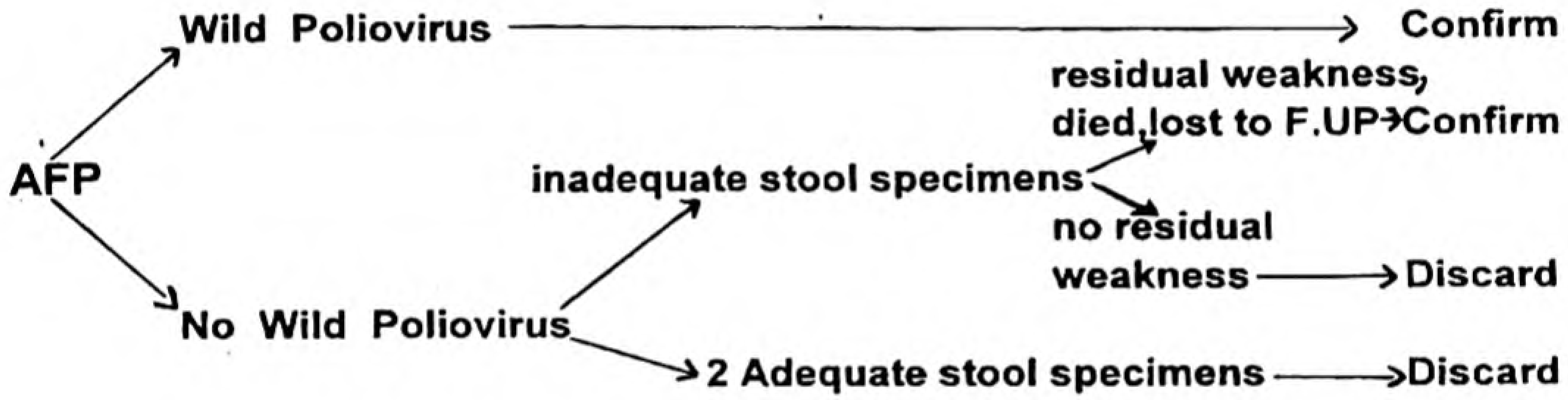
Mass immunization of children below 5 years of

TABLE II

Flow Diagram Of Case Investigation


Onset Of Paralysis
<7 Days
Investigation Of Suspected Case(<48 Hrs)
2 Stool Specimen collected <14 Days
<3 days
Specimens arrive National Lab.
<28 days
Results reported from Nat. Lab.
polio-virus isolates sent to ref.lab for intra typic diff.
Immediately
Outbreak response Immunization
60 day follow up examination
Final Classification of case (<12 weeks since et of parl.

Case Classification Scheme


Wild Poliovirus
Confirm
residual weakness, died,lost to F.UP
Confirm
AFP
inadequate stool specimens
no residual weakness
Discard
No Wild Poliovirus
2 Adequate stool specimens
Discard

age is conducted in the area to which the cases belonged after the stool samples from the said cases were collected. This is called the Outbreak Response Immunization (ORI), which should be carried out within 72 hours of the case investigation.

4. 60-day follow up:

Sixty days after the onset of paralysis every case of AFP is revisited to confirm the presence or absence of residual paralysis. It should be borne in mind that the entire classification scheme of AFP cases hinges on this 60-day follow-up. Cases of AFP are 'confirmed' as polio when:

i) they are associated with isolation of wild polio virus from the stool sample of the case.

ii) they have residual neurologic sequelae at 60 days after onset of paralysis.

iii) or if the patient died or got lost before the 60 days follow-up could determine whether residual neurological sequaelae were present[6].

The 3 indicators used to assess AFP Surveillance sensitivity are non-polio AFP rate, weekly zero (nil) reporting and percentage of AFP cases with 2 stool samples taken within 14 days after paralysis ensued. Based on the population composition of the J&K State 32 cases of AFP are expected to occur in whole State in one year. Against this expectation 101 cases of AFP have been reported already from almost all the districts of State, giving a total AFP rate of 3.2 as agaisnt the minimum expected 1. Currently about 86% of the reporting units are sending timely weekly reports including zero reporting.

Percentage of case with 2 stool samples taken within 14 days of onset of paralysis, is an effective indicator for assessing surveillance sensitivity, it not only monitors whether the cases are investigated in timely fashion but also whether 2 stools are adequately collected. This percentage should be 80% or more. Samples from the valley have been collected timely, and till date no wild virus has been isolated from any stool sample from the valley.

Analysis of the 1998- Surveillance Data

indicates that our State is also heading towards a polio free status. Though no wild virus has been isolated from any stool samples sent to the Kasauli lab till date, it is somewhat premature to claim that our State will overtake some other States in achieving polio elimination. The surveillance network is still to be extended to the border areas which may still be hardbouring some hidden foci of wild virus. It needs no over-emphasis to remember that, in an eradication programme the border States assume greater importance because of their proximity with different countries.

For on-time polio eradication routine OPV coverage needs to be maintained at above 90%, and the Pulse Polio & Outbreak Response Immunizations would have to be accorded highest priority so that the wild virus is completely replaced by the vaccine virus. Immunization coverage has to be boosted in the migratory populations in the State, especially among the immigrant labourers who mostly happen to come from Bihar, Bengal, Uttar Pradesh etc. (the areas which are still endemic for poliomyelitis and still go on reporting confirmed cases of poliomyelitis. The nomadic populations also would pose substantial challenge as they are apt to be missed because of their constant movement.

References:

1. Govt of India, Ministry of Health & Family Welfare, Child Health Division. PULSE POLIO IMMUNIZATION IN INDIA - OPERATIONA GUIDE, 1997; pg 28.
2. Indian Academy of Pediatrics, Polio Eradication Committee. ACADEMY TODAY, March 1998; pg 39-40.
3. Govt of India, Ministry of Health & Family Welfare, MCH Division. SURVEILLANCE OF ACUTE FLACCID PARALYSIS - FIELD GUIDE (Red Book); pg 4.
4. Ibid; pg 22.
5. Ibid; pg 7.
6. Ibid; pg 6.

With Best
Compliments From

KASHMIR PHYSIOTHERAPHY
&
REHABILITATION CENTRE

HRDC CAMPUS, POST OFFICE LANE, RAJBAGH, SRINAGAR-8
TELE : 450920

CONGENITAL URETHRAL ANOMALIES IN ANO-RECTAL MALFORMATIONS

Nasib C. Digray, M.S., M.Ch.; Yogeshwar Mengi M.S., M.Ch., H.L. Goswamy M.S.; D.R. Thappa M.S.

Abstract: Ten male infants of anorectal malformations (ARM) with congenital urethral anomalies are reported. Eight patients had hypospadias, whereas megalourethra and anterior urethral diverticulum were present in two children. Except for 4 patients with low ARM, all other 6 infants had various other congenital anomalies besides ARM. The incidence of hypospadias seems to be high (6%) as compared to available figure of 2.5% in the literature. Urethral anomalies like megalourethra may be associated with serious anomalies of other organ systems and need careful and early investigations.

Key words: Anorectal malformation, Urethral diverticulum, Imperforate anus, Megalourethra.

JK-Practitioner 1999; 6(2): 116-117

Introduction

Urethral anomalies except hypospadias are rare in patients of ARM. Megalourethra, urethral diverticulum, urethral duplication, anterior urethral valves, congenital urethral strictures, all have been reported. Patients with megalourethra and those with VATER (vertebral/vascular, anal, tracheo-esophageal, renal/radial) association may have serious life threatening anomalies, thus affecting the ultimate prognosis in these patients.

Patients and methods

One hundrend and forty patients of ARM were seen over a period of three years. Out of these 10 neonates had various urethral anomalies and from the basis of this report a throough clinical examination, a babygram and prone cross table lateral view[1] were done to classify the ARM as high, intermediate and low anomalies as per Wingspread classification[2]. All patients in follow up period had an ultrasonogram for detection of renal anomalies, whereas distal cologram was done in patients with colostomy. Cardiologists opinion was sought and echocardiogram done where there was a suspicion of cardiac anomaly. One patient, who had dribbling of urine with no obvious neurogenic problem, was detected to have anterior urethral diverticulum on retrograde urethrogram (RGU) as shown in figure 1.

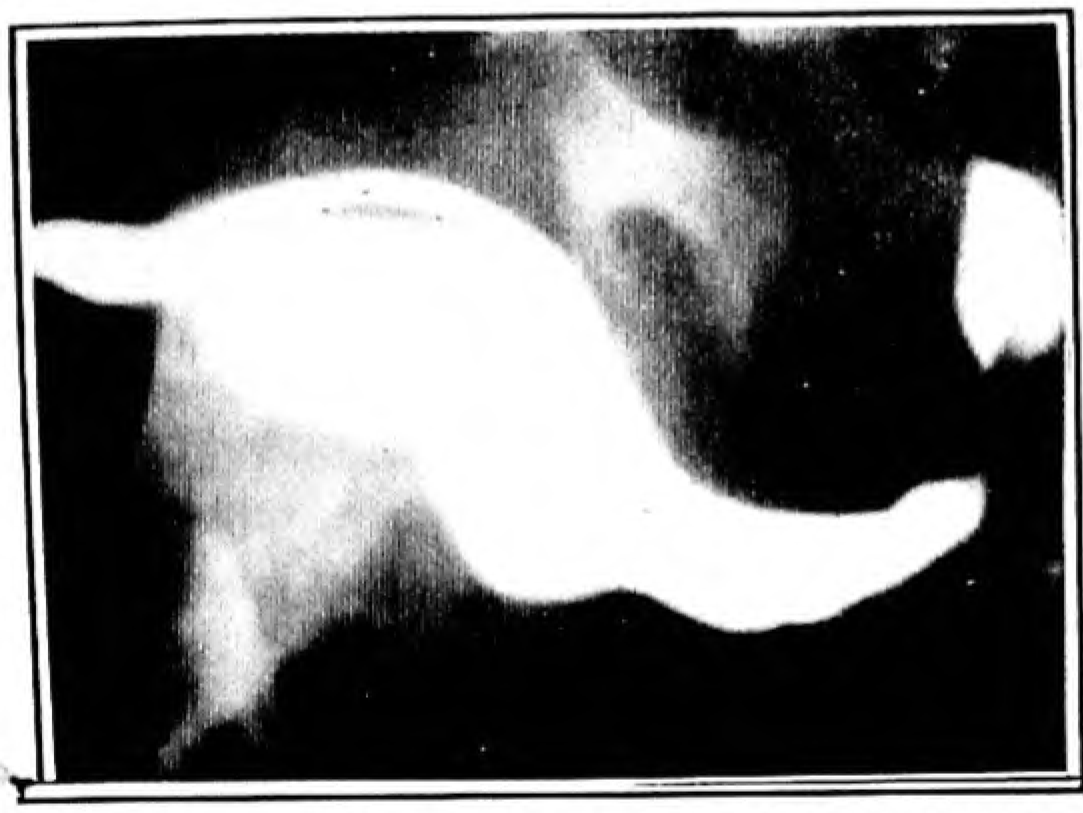


Fig.I. Retrograde Urethrogram in a patient of ARM showing anterior urethral diverticulum. No rectourethral fistula is seen

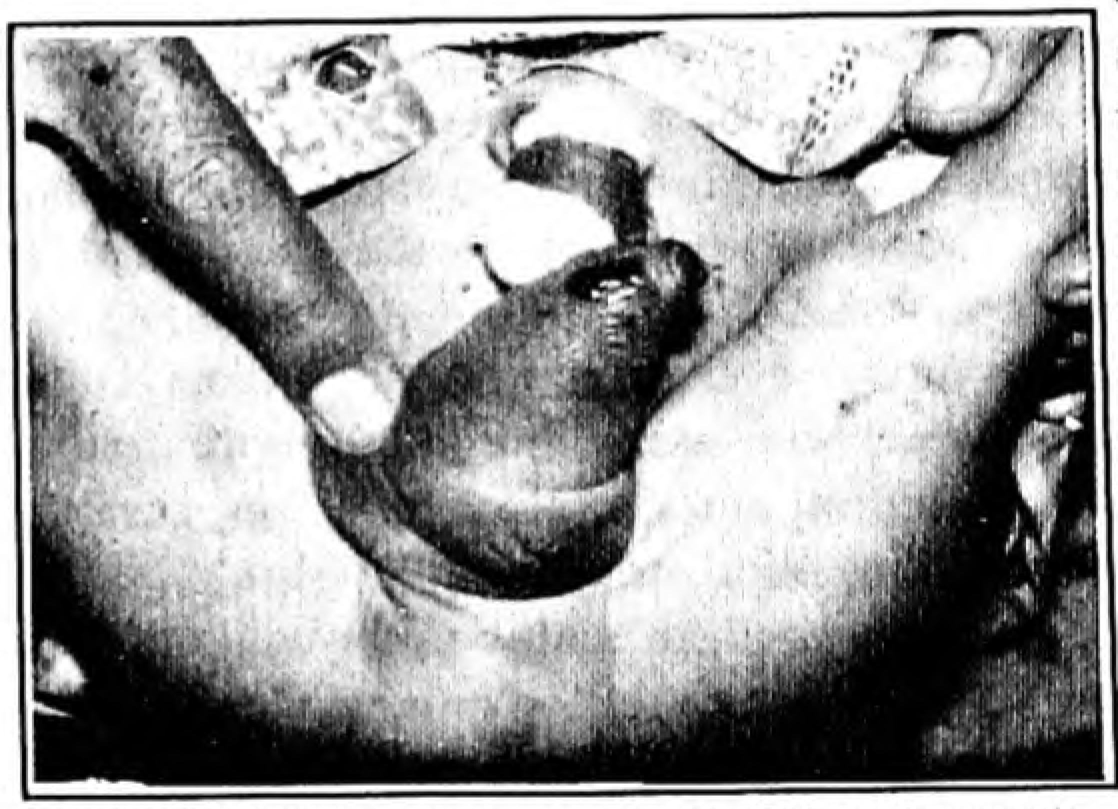


Fig.II. Clinical Photograph of a neonate with ARM showing megalo urothra, bilateral undecended testes and absent prepuce. Note specy of meconeum on pencile tip suggesting associated rectro-urethral fistula.

Results

The clinical data of infants with various urethral anomalies is summarised in table 1. Out of total 140 patients of ARM seen by us over a period of 3 years, 10(7%) were found to have urethral anomalies. Eight patients (6%) had hypospadias, whereas scaphoid megalourethra and anterior urethral diverticulum were significant anomalies present in one patient each. In patient of megalourethra the anomaly was very obvious on clinical examination (Fig. 2). An x-ray of abdomen, ultrasongraphy (US) and laparotomy revealed a pouch colon variety of high ARM and right renal agenesis. This patient died after pouch colon resection with colostomy and vesicostomy. The cause of death was septicaemia and renal failure. As is clear from Table 1, those patients with high/intermediate ARM have high incidence of not only of urethral anomalies, but

From the Department of Surgery (Paediatric Division) Govt. Medical College Jammu, India, (Digray, Mengi, Goswamy, Thappa)

Received June 1998 Accepted Febuary 1999

Corespondents: Dr. Nasib C. Digray Consultant Paediatric Surgeon, H.No. 220, Sarwal Colony, J&K State, India 180005.

Table 1 Showing various abnormalities in patients with ano-rectal malformations

Patient No	Urethral Anomaly	Type of ARM	Other Abnormalities.
1.	Megalourethra (Scaphoid)	High with (Pouch colon)	Rt. Renal agenesis B/L UDT, Meatal stenosis absent prepuce
2	Ant. Urethral Diverticulum	High	Left UPJO
3 4 5,6	Hypospadias	Low	Nil
7	Hypospadias	Intermediate	Syndactlyly
8	Hypospadias	Intermediate	TEF-EA
9	Hypospadias	High	Split scrotum, R UDT
10	Hypospadias	High	MMC

UDT = UNdescended testis. UPJO = Uretero-pelvic Junction Obstruction, MMC=Meningo=myelocele, TEF/EA=Tracheo=esophageal fistula with esophageal artresia

also of assciated other anomalies. None of our patients with urethral anomalies could be categorized to VATER associations.

Discussion

Genito-urinary anomalies may be present in 48% of the patients with ARM and this incidence seems to be directly related to type and severity of ARM and completeness of urological work up[3]. Whereas upper urological anomalies are more common, those of lower urological tract, involving urethra, are rare. Hypospadias, which is most common among these, may be present in 2.5% of cases with ARM[3]. Our figure of 6% seems to be high and needs further evaluation in more patients. Other abnormalities which are less common but more serious include megalourethra, anterior urethral valves, urethral duplications and congenital strictures of urethra[4,5]. Except for megalouurethra where the phallic abnormality is quite obvious to suggest the diagnosis on clinical examination, other patients with rare urethral anomalies need investigations like "voiding cystourethrogram" (VCUG) or RGU to document their presence[4,5]. Sometimes megalourethra may be obvious on pre-natal US along with other congenital abnormalities[6]. As pointed out earlier, the patient with high ARM are at more risk of having associated problems including those involving upper urinary tracts like renal agenesis, dysplasia etc.[7] A recent study[4] has shown that patients with VATER association have a high chance of serious urethral anomalies including megalourethra. Three patients of megalourethra in this study[4] died due to severe associated life threatening anomalies. Our one patient with megalourethra confirms this observation. The cause of urethral abnormalities in ARM seems to be a primary mesenchymal defect (megalourethra, urethral diverticulum, urethral stricture and anterior urethral valves) or a failure of septation process (H-type urethro-anal fistula, urethral duplication) as is the presence of TEF/EA and ARM. This concept although looks intriguing is not yet proved[8,9,10].

References:

1. Rao KLN, Mitra SK, Kataria S. prone-cross table lateral view: an alternative to invertogram in imperforate anus. Am. J Radiol. 1983; 140: 227-229.
2. Stephens FD, Smith ED. Classification, identification and assessment of surgical treatment of ano-rectal anomalies. Pediatr. Surg. Int. 1986. 1: 200-205.
3. Brock WA, Pena A. Cloacal abnormalities and imperforate anus. In: Clinical Pediatric Urology by Kelalis PP, King LR, Belman AB (Eds.) 1992. pp. 920-943.
4. Fernbach SK. Urethral abnormalities in male neonates with VATER association. Am. J. Radiol. 1991. 156(1): 137-140.
5. Firlit CF. Urethral abnormalities. Urol. Clin. N. AM. 1978. 5: 31-54.
6. Wu MH, Mu RC, Kuo PL et al. Prenatal ultrasonographic diagnosis of congenital urethra. Prenatal Diagnosis. 1995. 15(8): 765-768.
7. Belman AB, King LR. Urinary tract abnormalities associated with imperforate anus. J. Urol. 1972. 108: 823-824.
8. Bruce R, Alton D. Duplication of urethra with communication to rectum. Pediatr. Radiol. 1986. 16: 79-81.
9. de Varies PA, Friendland GW. Congenital H-type anourethral fistula. Radiology. 1974. 113: 397-407.
10. Stephens FD, Donnellan WL. H-type ano-urethral fistula. J. Pediatr. Surg. 1997; 12: 95-102.

HORMONAL AND SURGICAL MANAGEMENT OF CRYPTORCHIDISM

M. Saleem Tak M.S.; Rekha Patnaik M.Ch.; A.H. Zargar D.M.; Khurshid Aslam M.S.; Fayaz A. Sofi M.D.

***Abstract:** This study was conducted in 100 children upto age of 14 years in departments of Endocrinology and Paediatric Surgery, Sher-i-Kashmir Institute of Medical Sciences, Srinagar from September 1992 upto August 1994. The study included both unilateral and bilateral testes. A total number of fifty patients with bilateral undescended testes upto age group of 6 years were subjected to hormonal therapy with HCG 1000 IU via intramuscular route twice a week for 12 weeks. Complete descent of testes into the scrotum was observed in 20 percent patients remaining showed response with improvisation of position and increase in volume of the testes.Surgical management was performed with classical inguinal orchidopexy and showed best results 96 percent as compared to other procedures.A new inguinal canal by pass technique was employed in the testes located in the abdomen or near the deep inguinal ring. Success with procedure was noted in 85 percent cases. Fowlers Stephens Technique was done in 8 patients and out of that 3 testicular atrophies were noted.*

***Key words:** Cyptorchidism, Hormonal Therapy, Orchidopexy.*

JK-Parctitioner 1999; 6(2): 118-120

Introduction

Cryptorchidism occurs with incidence of 0.8 percent at one year of life and thus represents the most common disorder of male sexual differentiation. Long term sequalae of undescended testes include infertility and testicular malignancy. Despite the relative frequency of this disorder the etiology is unknown. Estrogen intake during pregnancy by mother in last trimester has been seen with increased incidence of undescended testes. Testicular descent is essential for normal spermatogenesis as the temperature in the scrotum is 1.5° C-2.0°C less than body temperature. Various locations of undescended testes include abdomen, inguinal canal, superficial inguinal pouch or the ectopic sites include femoral triangle and perineum. Various urological disorders like post-urethral valves, hypospadias are common associations. Anorchia or vanishing testes syndrome is seen in 3-4 percent patients. Patients with bilateral undescended testes with perineal hypospadias raise question of intersex. The treatment of undescended testes includes hormonal therapy with HCG, LHRH nasal spray and various surgical methods.

Meterial & Methods

This study was conducted in children upto age of fourteen years who attended departments of Endocrinology and Paediatric Surgery, Sher-i-Kashmir from September 1992 upto August 1994. A total number of one hundred children were taken into the study. The children were evaluated and a detailed history, examination, and routine investigations were carried out. Ultrasonography was used in the localization of impalpable testes. Fifty patients with bilateral undescended testes were subjected to hormonal therapy.

Injection via intramuscular route of human chronic gonadotrophin (LIFE) one thousand International Units twice a week for a period of 12 weeks. Children who received hormones were followed every one month for a period of one year and serial ultrasound were performed. Surgical management included fifty patients will unilateral undescended testes and those children who did not respond fully to hormonal-management. Three methods were used: (1) classical inguinal approach was used for testes located on USG or palpable near the inguinal region (2) new inguinal canal bypass procedure was performed for the testes which were located around the internal inguinal ring and intraabdominal testes. Testicular vessels were brought along with the testes in a straight line to the renal pedicle, inguinal canal bypassed new ring created over pubic tubercle so that the 3.5cms distance was gained, (3) Folwers-Stephens Technique was used in a very highly placed testes i.e., when associated with short testicular vessels. High ligation of testicular artery was done only after temporary clamping of testicular vessels for a short period and the colour of testes observed, in cases where no colour

From the Departments of Paediatric Surgery (Tak, Prof. Patnaik) **Endocrinology (Prof. Zargar) Surgery** (Aslam) and Medicine (Sofi) **SKIMS, Soura, Srinagar Kashmir India.**

Received July 1998 Accepted February 1999

Correspondence to : Dr. Saleem Tak, Deptt. of Paediatric Surgery, SKIMS Soura, Srinagar 190011. GPO Post Bag 27.

change was observed the procedure was done. The basic of the procedure was defferential arteries could nourish the testes when dissected carefully.

In every case the testis after reaching the scrotum was burried in subdartos pouch created at the base of the scrotum in every patient.

Observation

Effects of Hormonal Therapy

A total number of fifty children with bilateral impalpable undescended testes upto age of 6 years were subjected to hormonal therapy with HCG 1000 IU twice a week for 12 weeks. Comparison was made with same age group and similar number of children with a palacebo. Results were seen on follow up and with help of serial ultrasounds. Twenty percent of patients showed complete descent in the scortum, thirty four percent children showed their testes which became palpable; in other 26 percent resulted in increase in size and improvization in their position and 20 percent showed no response.

Table-1: Showing Response to Hormones in Comparison to Placebo

Hormonal regime	Total No. of pts. testes	Complete descent pts Testes (%)	Palpable pts. Testes (%)	Increase in size pts. Testes (%)	No effect pts. Testes (%)
HCG 1000 IU twice/wk for 12 weeks	50 100	10(20) 20	17(34) 34	13(26) 26	10(20) 20
Placebo twice/wk	50 100		6(12) 12	5(10) 10	39(78) 78

No side effect was noted in the patients.

Surgical techniques

Total number of ninety patients which included 50 children with undescended tests and forty children which failed to respond fully to hormones. Three methods were used:

i) Classical inguinal approach with Dartos Pouch technique was performed in children with undescended testes who had palpable testes or localized testes on USG. A total number of 62 patients were subjected to his procedure. All the patients were followed up in OPD Clinic. Two patients developed testicular atrophy, three patients developed wound infection. Rest of the patients behaved normal.

Table-2: Showing three Surgical Techniques and Results

Procedure	No. of patients	No. of pts with complete descend(%)	No. of pts. with incomplete descend (%)	Atrophy
Classical inguinal approach	62	60(96.43)	1	1
Inguinal canal by-pass procedure	20	17(85.00)	2	1
Fowlers & Stephens	08	05(62.50)		3

(ii) Inguinal Canal by-pass technique:

This procedure was performed on 20 patients. 17 patients had their testes normally in the scrotum. Two patients showed their testes at level of public tubercle and one patient got testicular atrophy.

Fowler's Stephen's technique was performed on 8 children with intra-abdominal testes located very high and their testicular vessels too short to get these into the scrotum. High ligation of testicular vessels was performed on these. Five patients got success and three patients developed testicular atrophy.

Discussion

The incidence of cryptorchidism is 0.2-0.8 percent at one year of life (Scorer & Farrington). The associated anomalies include hernia, hypospadias and meatal stenosis. In our study 2 cases of hypothyroidism were seen (Farrington & Kerr). Gross & Jewet 1956 in a study of 1222 operations showed 3 percent absent testes and one percent perineal tests.

Table-3: Incidence of Urological abnormalities associated with undescended testes quoted in literature

S.No.	Name of the author	Year	No. of cases Studied	No. of cases with urological anomalies
1.	Farrington & Kerr	1969	45	06
2.	Donohoe, Utley & Maling	1934	100	14
3.	Watson, Lenonx & Gangai	1974	400	52
4.	Waaler & Maurseth	1976	166	02
5.	Present study	1992-94	100	06

Ultrasonography was done for localization of undescended testes and effect of hormones over the testes. Our results were 74 percent. The results were comperable to Wolverson et al & Klunderoff et al (1983, 1985).

Hormonal therapy was employed in fifty children with injection of HCG. Our results (complete descend) was 20 percent. The study conducted of Wespi (1954), Knorr (1971) showd 32 percent results in terms of complete descend. Moul & Belman (1987) showed poor results. Thompson and Heckel (1983) showed 65 percent results in terms of complete descend. These results are in contrast to our study, but the selection of patients has been indiscriminate and the authors had included retractile testes also in the study. Ehric et al (1969) reported results with gonadotrophin causing descent in 38 percent of bilatral and 11 percent in unilateral cases. De-Munickkeizer-Schrama et al (1986) in a double blind placebo controlled study of 252 boys who were treated with LHRH results were 8 percent, but second dose showed lot of improvement in results upto 75 percent.

With et al showed 37 percent. Urban et al upto 32 percent.

Surgical management The classical inguinal approach used by us in the study in Similar to Rajfer (1982), Wooley 1982 and Sheldon 1985. In our study one post-operative testicular atrophy was observed with classical groin approach. Arid (1949) showed 40 percent testicular atrophy post-operatively. But Synden and Chaffin 1955 who got 2 percent atrophy similar to our study.. Inguinal by-pass technique was used by Jones & Bagley (1979) with 99 percent results comparable to our 85 percent results. Chatterji and Roy (1985) utilized similar technique got 75 percent results.

Saw et al (1992) showed 95 percent testes reached the scrotum included 70 percent abdominal and 94 percent cannalicular testes.

References:

1. Ashbay EC, Maldescended Testes. Recent Adv Surg 1980; 1015 ed. 33.
2. Benson CD, Lotfi MW. Pouch technique in surgical correction of cryptorchidism in infants and children. Surg 1967; 62(5): 967.
3. Chatterji SK, Roy S. The impalpable testes-results by a new operative approach. Surg J India 1985; 2: 273-77.
4. De-Muinickkeizer-Schrama SMPF, Hazebrock FWJ, Matroos AW et al. Double-blind placebo controlled study of luteinizing hormone releasing hormone nasal spray in treatment of undescended testes. Lancet 1986; 19: 876.
5. Elder JS. The undescended testes: Hormonal and surgical management. Surg Clin North Am 1988; 68(5): 983.
6. Farrington GH, Kerr IH. Abnormalities of upper urinary tract in cryptorchidism. Br J Urol 1969; 47: 77.
7. Gross RE, Jewett TC (Jr). Surgical experiences from 1222 operations for undescended testes. JAMA 1956; 160:634.
8. Kullenderff CM, Hederstorm E, Fosbarg L. Preoperative ultrasonography of the undescended testes. Scand J Urol Nphrol 1985; 19: 13-15.
9. Moul JW, Belman AB. A review of surgical treatment of undescended testes with emphasis on anatomical position. Jr Urol 1988; 140: 125.
10. Rajfer J, Handeslman DJ, Sweldtoff RS, Hurtvitz R et al. Hormonal therapy of cryptorchidism. N Engl J Med 1986; 312: 466.
11. Shapiro SR. Hormonal therapy of cryptorchidsm with HCG. Urol CLinic N America 1982; 9: 405.
12. Urban MD, Lee PA, Lanes J, Claude J. HCG stimulation in children with cryptorchidism. Clin Paediatrics 1987; 26(10): 512.
13. Wolverson MK, Jagannadharo B, Sundram M, Riaz MA et al. CT in localization of impapable crytorchid testes. AJR 1980; 134: 725.

A GP Finds a new treatment for migraine

Dr. Ghulam Nahami a GP in Sheffield South Yorkshire framed a simple questionnaire asking blood donors how they felt after donating blood.

His observations:

Dr. Ghulam Nahami

- Of nearly 2,100 blood donors questioned, 7 per cent reported feeling better after giving blood.
- One per cent of blood donors felt worse.
- Of the 142 patients who felt better after giving blood, 13 per cent reported that their migraines were less frequent and less severe.

Details in GP Medicine Section - Anecdotal Medicine June 20 1997.

SIMPLE LIGATION FOR APPENDECTOMY A BETTER CHOICE THAN STUMP INVAGINATION

M.S.Misgar, MS; Ghulam Hussain, MS; Mufti Mehmood, MS; Arshad Shafi, MS; Ab. Rashid Lone, MS.

Abstract: *100 cases of appendectomy were performed from Jan. 1995 to Jan. 1997. A comparative study of two methods of treatment of appendicular stump (a) simple ligation (b) stump invagination was performed in two groups of fifty (50) each. Total hospital stay was recorded in both the groups.It was concluded in the present study that simple ligation is simple procedure, low cost, takes less operative time, less post opertive complications and reduced hospital stay as compared to stump invagination.*

Keywords: *Simple ligation, Stump invagination.*

JK-Practitioner 1999; 6(2): 121-124

Introduction:

Appendectomy accounts for about 1% of all surgical operations Lewis et al 1975[1]. Appendectomy is the most commonly performed emergency abdominal surgical procedure Co-operman Mare 1983[2].

The prefered methods used now-a-days for the management of the appendiceal stump are:

1) Simple ligation and
2) Ligation with inversion of stump.

Keeping in view the divergence of opinion, the present clinical problem has been contemplated to review the advantages and disadvantages of each technique from the stand point of (a) technical simplicity (b) cost effectiveness and (c) complications and to choose a preferable technique.

Material and Methods:

The present clinical study was taken on 100 cases of acute appendicitis in the department of Surgery, Govt. Medical College, Srinagar, from January 1995 to Jan. 1997. All the cases of acute appendicitis were subjected to emergency appendectomy. A comperative study of two methods of treatment of appendicular stump e.g. (1) simple ligation and (2) stump invagination was made. The case were divided into two groups of 50 each.

The cases diagnosed as acute appendicitis were subjected to emergency appendectomy. In case where the diagnosis was more certain McBurney's grid iron incision and Lanz incision were used and in patients with doubtful diagnosis a right lower para median incision was used. Appendectomy with reference to the treatment of appendix stump was performed in the light of following two methods.

Simple Ligation (Group 'A')

The appendicular base was crushed with appendicular crushing forceps and a ligature of 2° silk was tied over the crushed area and appendectomy performed by cutting flush along the inferior surface of appendicular crushing forceps. The mucous membrane of the gut and of appendix stump was cleaned with sponge and spirit. Haemostasis was secured and last two feet of ileum were inspected for any incidental lesion especially Meckles diverticulum.

Stump invagination (Group 'B')

The appendicular base was crushed with appendicular crushing forceps and a ligature of 2° chromic catgut was tied over the crushed area. A purse string sero-muscular suture of 2° chromic catgut was inserted into the caecal wall around the base of the appendix and appendectomy was performed by cutting flush along the inferior surface of appendicular crushing forceps. The stump was invaginated and purse string suture tied.

The total operation time was noted and recorded in both the methods. Patients were watched for any post-operative complications and treated well in time. The wound was examined on 3rd postoperative day. In case of wound infection a bacteriological swab was taken and sent for smear and culture sensitivity examination and accordingly antibiotics were changed. Majority of patients were discharged from 4 to 6 days and called back for removal of stitches on 7th postoperative day.

Total hospital stay was noted down and recorded. Patients were advised to attend follow up clinic every month of it and when needed, so as to note any complications arising from the procedure.

Observation:

A total of 100 cases were studied in the Deptt. of

From the Department of Surgery (Prof. Misgar, Hussain, Mehmood, Shafi, Lone) **GMC, Srinagar, Kashmir**

Received January 1998 Accepted March 1999

Correspondence to.: M.S.Misgar, Head Deptt. of Surgery, GMC Srinagar.

Surgery, Government Medical College Srinagar, in period of two years from Januuary 1995 to January 1997. Comprising two groups viz. Group 'A' and Group 'B' each group consisting of 50 patients. Group wise distribution depicted in table I.

Table I: Showing distribution of number of patients with respect to type of appendectomy and treatment of stump

Group	Procedure employed	Diagnosis	Type of app.	No. of Cases	%age
'A'	Simple ligation	Acute app.	Emergency app.	50	50
'B'	Stump invagination	Acute app.	Emergency app.	50	50
	Total			100	100

60 cases were males and 40 cases were females.

Male to female ration was 3:2.

Incision:

In 50 patients Lanz's incisions was made, in 30 patients MacBurney's gird iron incisions was made and in 20 patients (20%) right lower paramedian incisions was made.

Operative findings:

Operative findings were observed under two broad headings:

1. **Peritonitis**
2. **Condition of appendix**

1. **Peritonitis:** 15 patients (15%) had generalized peritonitis and 20 patients had localized peritonitis.

Table II:

Gross condition of appendix and the treatment of apendicular stump is briefed in following table

Condition of appendix at (gross naked eye examination)	No. of cases	%age simple	Group A stump ligation	Group B stump ligation
Inflammed appendix	80	80	40(80%)	40(80%)
Perforated appendix	10	10	5(10%)	5(10%)
Normal appendix	5	5	3(06%)	3(06%)
Gangrenous appendix	5	5	2(04%)	2(04%)
Total	100	100	50(100%)	50(100%)

Treatment of appendicular stump:

Group 'A' simple ligation consisted of 50 patients with emergency appendectomies and group 'B' (stump invagination) consisted of 50 patients which were also emergency appendectomies.

Suture material used for treatment of appendix stump:

In group 'A' cases 2° silk was used for ligation of appendicular stump and in group 'B' cases 2° chromic catgut was used for transfixing the appendix stump and same material was used for purse string suture.

Treatment of cut end of stump:

After appendectomy was performed, in both the groups the mucous membrane of the cut end was cleansed with sponge and spirit.

Use of Drain:

In total of 35 cases (35%) in this study having concomitant localized (20 patients) and generalized peritonitis (15 patients) after thorough lavage and mopping the peritoneal cavity dry, a corrugated rubber drain was used, which was brought out through separate stab incision. These patients were equally distributed in two different groups (A&B) at study.

Type of treatment of stump (appendicular)	Operative procedures No. of cases at study	Mean Operativetime
Simple ligation (Group A)	50	40 minutes
Stump invagination (Group B)	50	50 minutes

Contents of vermiform appendix:

All the appendix specimens were slitted longitudinally to see the contents in its lumen.

40 specimens were empty, 28 cases contained pus and 32 specimens contained fecolith. This shows that 32% of cases had obstructive appendicitis.

Postoperative complications compared in two groups:

1) **Postoperative pyrexia:**
9 patients from group A 11 patients from group B developed postoperative pyrexia. In all 18% from simple ligation and 22% from stump invagination developed post-operative pyrexia.

2) **Postoperative pain:**
No significant difference in postoperative pain in two groups was observed.

3) **Removal of drain:**
Drains were used in 35% of patients in this study viz. group A cases 15 patients and in group B eases for 15 patients (15%). It was observed that drain was removed earlier in simple ligation group of cases as compared to stump invaginaton group of cases.

4) **Wound infection:**
15% of patients (15 patients) developed wound infection from whole series of 100 patients. Five cases (10%) were from group A and 10(20%) cases from group B. It was observed that incidence of wound infection was more in stump invagination group as compared to a imple ligation group.

5) Wound infection in relation to incision used:

S.No.	Incision used	No. of patients	No. of patients who developed infection	%age
1.	Lanz's incision	50	2	4
2.	Macburney's incision	30	3	6
3.	Right lower paramedian incision	30	4	20
	Total	100	9	30

Table III:
Showing incidence of wound infection in relation to incision used

It was observed that majority of patients who were opened by right lower paramedian incision developed wound infection.

6) Wound infection in relation to age of patients:
It was observed that rate of infection was more in extremes of the age (0-10 years and 51-60 years).

7) Intestinal observation:
Two cases of intestinal obstruction were observed in postoperative period. Both cases belonged to stump invagination. One case developed intestinal obstruction in the form of intussusception following appendectomy. Heparatomy was performed and patient recovered.

8) Intraperitoneal abscess:
4 patients (4%) developed pelvic abscess in whole study. Patients (3%) in group A cases and 3 patients (3%) in group B cases.

9) Faecal fistule:
Postoperative faecal fistule was observed in one patient in group B cases. None of group A cases developed faecal fistula.

10)Histopathology:
The hospital stay on average was 4 to 5 days (less) in group A cases and 6 to 7 days in group B cases.

11)Mortality:
Mortality in both groups was zero.

Discussion:

Two methods of treatment of appendicular stump were employed in present study. Patients were equally divided in two groups of 50 patients. Group A called simple ligation group and group B as stump invagination group The two groups were compared regarding mean operating time, mean hospital stay and postoperative complication.

Oschner A Willy G, (1937), Walers. DAK et al (1984), also compared the two standarad methods of treatment of appendix stump. Sinha AP (1977), after analysing records over 5 years in Secotland from 1970-74 found that most surgeons used dmajor simple ligation technique in all cases of established localized generalized peritonitis.

Mean operating time:

In this study the mean operaive time was 40 minutes in simple ligation and 50 minutes for stump invagination.

Oschner A, Lilly G (1937), also say that simple ligation can be completed with less manipulation and greater rapidity than other methods.

Ergston L and Fenyo G (1985) in their study also found that median operative time was 40 minutes in simple ligation and 45 minutes in stump invagination.

Contents of vermiform oppendix:

In this study the contents of the appendix when they were slit open was 40% (empty) 28% (puss), 32% (fecolith), Hence 1/3 of the present study were obstructive in nature. Similar findings were observed by Kelly and Hundon (1905), Arthun, Harding Rains, AJ and Mann CV (1990), in Love and Baily short practice of surgery.

Postoperative complication operated in 2 groups:

1) Postoperative pyrexia:
In this study 7% (7 patients) of group A and 11% (11 patients) from group B and overall 18% from simple ligation and 22% from stump invagination group developed postoperative pyrexia respectively. Although the study is small, yet we have not been able to find out definite cause for postoperative fever. The possible causes as reported by Kinglay, DPZ (1969), could be infection around the stump either lying free in cavity but walled off or within inversion stump.

2) Postoperative pain:
No surgical difference was observed as regards postoperative pain.

3) Wound infection:
Overall wound infection was reported as 15%. It was found more in group B cases (20%) and 10% in group A cases. Sinha A.P. (1977), reported a wound infection rate as 16.11% in stump invagination (Group B) and 5.77% in simple ligation.
Findings in this study corresponded well with that of Sinah. Overall wound infection was more in perforated and gangrenous appendix than acute inflammed appendix. Wound infection was more in those cases where R.L.incision was used than those

operated by small incisions like Lanz's or Macburney's incision. Gilmore, OJA and Martin T.D.M. (1974) says that incidence of postoperative wound infections is effected by skill of surgeon and technique of surgery.

4) **Intestinal obstruction:**

In this study two cases of obstruction were detected. Both cases belonged to Group B-stump invagination group. Both cases developed colocolic intussusception.

Clavland, G (1953) has reported six cases of intussusception following appendectomy in the literature. Clavland, G (1953) and Mayo (1934) stated that this was one of the reasons why he did not practise invagination of stump.

5) **Intraperitoneal abscess:**

4 cases of intraperitoneal abscess were observed in this study, one belonged to simple ligation group and 3 belonged to stump invagination group. Sinha A.P. (1977), reported an incidence of postoperative pelvic abscess of 0.94% in stump invagination and 0.23% in simple ligation group. The present study is in confirmity with findings of Kingsley DPE, Sinha AP etc. The increased incidence of intraperitoneal abscess was found in perforated appendicitis owing to dependent portion of pelvis.

6) **Faecal fistule:**

Postoperative faecal fistula was observed in one patient of stump invagination and none from group 'A' cases. The patient responded to conservative treatment, fistula healed, patient recovered and discharged from hospital. Incidence of faecal fistule has been reported as 2 to 4% in different studies as quoted by Beldwin in (1932) and 1.1% as quoted by Colp. Ralph (1926), Baldwin (1932) objected to use of purse-string suture on the basis that it might interfere with the blood supply of caecal wall and cause faecal fistule. As it belongs to stump invagination group it interferes with blood supply of caecal wall caused by purse string suture in odematous friable caecum.

Mortality in both cases was zero:

Hospital stay:

Average hospital stay in stump invaginal group was 6-7 days in group B and 4-5 days in group A cases. This hospital stay was less in simple ligation group.

Sinha AP (1977), while studying 643 cases found that hospital stay was shorter in simple ligation group than stump invagination. Our hospital being charity hospital, shorter postoperative stay matters lot in terms of patient turnover and cost effectiveness.

Cost effectivness:

In simple ligation group 2° silk was used for ligation of stump, no purse string suture was given, no catgut was used thus saving money etc.

Summary and Conclusions:

Although our study is small (100 cases) we have been able to make following observations.

1. Simple ligation is simple precedure compared to stump invagination.
2. Low cost involved in simple ligation than stump invagination.
3. Operating time, less in simple ligation than stump invagination.
4. Postoperative complication are less in simple ligation.
5. Hospital stay is less in simple ligation than stump invagination.

References:

1. Lewis, F.R. et al: Appendicitis, A critical review of diagnosis and treatment in 100 cases, Arch. Surg. 110: 667: 1975.
2. Cooperman, M.: Complications of appendectomy, Surg. Clinical North America: 1983; 63: 1233-1247.
3. Senn. N.: A plea in favour of early laparotomy for ulcerative appendices with report of two cases. JAMA 1889; 13: 630.
4. Kelly, H.A> and Hurdon, E.: The vermiform appendix and its disease, Philedelphic WD Saunday and Company 1905.
5. Deaver JB: Appendicitis-its history, anatomy, clinical aetiology, Pathology, Symptomology, diagnosis, prognosis, treatment, tech of opouh complicate and sequle philadelphic Blakiston's Sons and Co. 1914.
6. Schwartz, SI and Ellis H.: Maingots abdominal surgery, 9th Ed, 1996; Vol 2. p. 653-977.
7. Harding RAJ and Mann, VC.: Baily and Love's short practice of surgery ELBS ed, EPCC Hazell books, Aylesbury books England, 20th Ed. 1990; p. 1090-1109.
8. Rogers, H. and Faxon: Statistical study of 671 cases of appendiceal peritonitis New Eng. J.Med. 1992; 226; 707-717; 745-753.
9. Berry, J.J. and Malt R.A.: Appendicitis wears its centenary, Anals of surgery, 1984; 567-575.
10. Ochner, A.S.: A handbook of appendicitis, Chingo, 1902, G.P. Gerhardt.

CANCER AND PREGNANCY

Gangadharan V.P, D.M.; Chithra Thara. K, M.D.; Preetha Soman, M.B.B.S.

Abstract: *The diagnosis of malignancy in pregnancy is a complex problem involving two lives. Treatment depends on the period of gestation, type of malignancy, aggressiveness of the tumor and stage of disease. Abdominopelvic radiation is avoided at any stage of pregnancy. Administration of cytotoxic drugs are relatively safe in second and third trimester. We report 13 cases of cancer with pregnancy treated at Regional Cancer Centre, Thiruvananthapuram, India, during 1990-1996. These are probably the first cases of osteogenic sarcoma and nasopharyngeal carcinoma reported during pregnancy.*

Key words: *Cancer and pregnancy, Chemotherapy, Teratogenecity.*

JK-Practitioner 1999; 6(2): 125-129

Introduction:

The diagnosis of malignancy in pregnancy is associated with much anxiety and distress and poses difficult challenge to the women, her family and the treating physician. Two lives, that of patient and fetus are involved in the game. Maternal survival may be compromised due to delayed diagnosis, complications and treatment. Delayed diagnosis due to masking of symptoms related to tumour development is common in colonic and other gastro intestinal cancer[1]. Large cystic intra abdominal ovarian tumours may mimic a cystic enlarged gravid uterus. Pregnant women has a 2-5 fold increased risk to present with metastatic breast cacer due to late diagnosis. Proliferation and decreased apoptosis of tumour cells may be the effect of various cytokines and hormones related to pregnancy. It could be speculated that following the initiation event for cellular proliferation, the maternal immune system may be more tolerant to the development of tumours similar to the tolerance of paternal allo antigens[2]. Two cases of colon carcinoma diagnosed during pregnancy were subsequently demonstrated to have over expression of P53[3]. DNA damage causing genetic stress as on path way for tumour development or mutations in the second allele of the P53 gene in a heterozygotic patient as a second path way for tumour development may be correlated with increased expression of P53.

In contrast, a pregnant woman has a higher chance of being diagnosed with stage I cervical cancer, during the pregnancy related regular obstetrical examination. In addition, there is ample data that pregnancy is protective against ovarian cancer[4]

It may be necessary to medically terminate the pregnancy to hasten treatment, or it may end up in miscarriage due to treatment. This is a decision since the mother can have permanent sterility or diminished reproductive function following treatment. Donegan[5], of the centres for disease control, reported that 1:118 women with cancer are pregnant. He commented that the two primary conditions of immunologic tolerance in seemingly intact immune systems are cancer and pregnancy[6], with breast and cervical cancers being the most frequent, each accounting for approximately 25% of the total. In a pregnant women with metastatic adeno carcinoma, a breast primary should be strongly suspected. Rothman et al[7] reviewed the literature and reported 35 cases of maternal malignancy with placental or fetal involvement, commonly reported being malignant melanoma followed by leukemia/lymphoma. Overall, it appears that fetus and placenta are resistant to metastasis from a maternal tumour, although few more cases have been reported.

The precise incidence of leukemia in pregnancy is unknown. It is thought to occur in only one per 1,00,000 pregnancies annually[8]. Overall, lymphoma is the fourth most frequent cancer among pregnant women. The frequency of Hodgkins lymphoma during pregnancy is estimated at 1/1000 to 1/6000[9] but that of non Hodgkins lymphoma (NHL) has not been established.

Based on the primary disease and duration of pregnancy, the evaluation and treatment may have to be modified, but should never be compromised.

Materials and Methods:

We report 13 cases of cancer with pregnancy treated at Regional Cancer Centre, during 1990-1996. The

From the Regional Cancer Institute, Thiruvananthapuram, India (Prof. Gangadharan, Thara, Soman)

Received September 1998 Accepted December 1998

Correspondence to : Gangadharan V.P., Head, Division of Medical Oncology, Regional Cancer Centre, Thiruvananthapuram - 695011, India

maximum number of patients in our series turned out to be acute leukemia, attributable to the disparity in referral pattern. These are probably the first cases of osteogenic sarcoma and nasopharyngeal carcinoma reported during pregnancy. Prognosis, treatment and toxicity to both mother and fetus were discussed in detail with the patient prior to therapy. Outcome of pregnancy and disease are analyzed specifically.

Discussion:

The effect of pregnancy on the growth and spread of cancer has been debated for decades. Some believed that pregnancy augments neoplastic growth and metastasis and has a negative effect on the prognosis[9,10,11]; others suggested no effect[12,13,14] or even a protective effect for the patients[15,16]. This controversy was active in breast cancer and malignant melanoma. Till today, there is no convincing data to suggest that pregnancy adversely affects the biology, prognosis or treatment of these controversial malignancies.

The data of pregnant and non pregnant leukemia patients were comparable with regard to complete remission rates. Complete remission of 72% and 76% reported in 45 pregnant women with Acute myeloblastic leukemia (AML) and Acute lymphoblastic leukemia (ALL) respectively[17] compared favourably with published results in similar non pregnant women[18,19] Comparison of relapse free survival and survival between the two groups has not been possible in acute leukemias due to inadequate and incomparable data. Thus, there is no available evidence, suggesting that pregnancy in itself alters the incidence, natural history or prognosis of acute leukemia. However, the median survival of 38 months reported for the 202 pregnant women[20] with Chronic myeloid leukemia (CML) do not significantly differ from the non pregnant individuals.[21]

Barry et al[22] and Gobbi et al[23] reviewed the association between pregnancy and Hodgkins disease. They concluded that pregnancy did not exacerbate the disease or adversely affect the mean survival. Paucity of data eludes any such conclusions in NHL. However, it is reported that NHL in pregnancy is most commonly associated with aggressive histology and disseminated disease[24]. There is a dramatic rapidly deteriorating course described in Burkitt's lymphoma with breast[25,26] and ovarian involvement[27].

Gestational trophoblastic disease (GTD) is constituted by a spectrum of interrrelated diseases including benign vesicular mole, invasive mole and chorio carcinoma. They vary in their capacity to invade and spread, but has a high cure rate even in a disseminated disease[28]. A full discussion on this entity is beyond the scope of this article and the present discussion will confine to a viable pregnancy associated with chorio carcinoma. This is rare and only 31 cases have been reported so far[29]. The disease tends to be widely disseminated at the time of diagnosis. Serum β HCG levels are usually raised as in other cases of chorio carcinoma, one case being reported with normal β HCG level[30]. Early diagnosis and adequate aggressive chemotherapy is critical for mother and fetus.

Majority of the ovarian tumours associated with pregnancy are benign[31] and the incidence of malignant ovarian tumours associated with pregnancy are only one case per 17,000 to 38,000 term deliveries[32]. Approximately two thirds of these ovarian cancers are of epithelial origin and are low grade/border line tumours. There is an increased incidence of tumour torsion or rupture presenting as acute abdomen[33]. Acute presentations are especially common in dysgerminomas.

The influence of pregnancy on osteosarcoma and nasopharyngeal carcinoma are unknown. Our patient with osteosarcoma had a bulky primary lesion with no dissemination. In contrast, the lady with nasopharyngeal carcinoma presented with a disseminated bone disease, in addition to the advanced primary. That data on the effect of leukemia as such on pregnancy is lacking in literature. This may be because of the facts that leukemia appeared frequently during the later stages of pregnancy and that survival of an untreated acute leukemia would be less than two months. The effect of anti leukemic chemotherapy on pregnancy is discussed later.

Pregnancy is unaffected by the presence of Hodgkin's disease with no effect on the course of gestation and delivery, or on the incidence of spontaneous abortions or prematurity[34]. NHL adversely affects pregnancy, most have died from progressive disease, undelivered or shortly after an abortion[35]. The first successful pregnancy associated with advanced NHL treated with aggressive combination chemotherapy was reported in 1977[36]; since then a number of success stories has flooded the literature[37,38].

Much of the concern on the effect of ovarian tumour on pregnancy relates to the controversy of extensive exploration during the course of pregnancy. Failure to remove ovarian masses greater than 6cm in diameter during mid pregnancy can lead to severe third trimester complication, including obstructed labour. None of the 15 patients reported by White[39] who underwent ovarian surgery in pregnancy developed premature labour and delivery. Neonatal mortality from prematurity is significantly increased when surgery is delayed until the third trimester[40].

Adverse effects of ionising radiation of fetus-teratogenic, growth retarding and lethal effects, are concentrated in the first 6 weeks of gestation, the period of organogenesis. There is no evidence that diagnostic radiation exposure below 0.05 Gy at any time during gestation cause any such adverse effects in human fetus. However, ultrasound examination can be advocated as a substitute for X-ray procedures wherever feasible. The natural expectation for the birth or a markedly handicapped child at the end of a normal pregnancy is about 1/30. The risk from medical diagnostic procedures would seem to be at least 30 times smaller than this[41]. Therapeutic radiation to abdomen is contraindicated at any stage of pregnancy. Fetal exposure of greater than 10 rad in the first trimester has been recommended as an indication for therapeutic abortion[42].

Physiological changes in pregnancy should be remembered whenever the pharmakokinetics of chemotherapeutic agents are discussed. Drug distribution is affected due to the increased plasma volume and decreased albumin levels. There is a rapid clearance of the drugs from the body due to rapid hepatic oxidation and increased renal clearance. Whether amniotic fluid can function as a third space for drugs is not known. However, there is no data on dose modification of chemotherapeutic drugs in pregnancy.

Chemotherapeutic drugs can cross the placenta and cause severe teratogenic effects in fetus especially during the first trimester of pregnancy[43,44]. It is worth noting that folic acid antagonists aminopterin[45] and methotrexate[46] have been more commonly associated with fetal abnormalities when given in the first trimester. Hence, folic acid antagonists should be avoided in the first trimester. There are only 2 cases of malformation in 50 cases receiving alkylating agents alone. Procarbazine was an agent in 4/7 malformations reported with combination chemotherapy. There is no data available on vincristine; vinblastine being a relatively safe drug in first trimester of pregnancy. In contrast to these first trimester findings, administration of cytotoxic drugs are relatively safe in second and third trimester, with no evidence of an increased risk of terratogencity.

Antineoplastic agents can also cause low birth weight, intrauterine growth retardation, spontaneous abortion, premature birth and major organ toxicity. Such effects are not limited to exposure in the first trimester. 45% of exposed fetus were of low birth weight[47].

Sutcliff[48] reported 82 spontaneous and therapeutic abortions among 218 pregnancies associated with cytotoxic drugs. Several cases of neonatal bone marrow hypoplasis have been reported following chemotherapy during second or third trimester[49], one of them had neonatal hair loss at 10 days[50]. Anhydramnios with cessation of fetal growth has been reported following a course of chemotherapy with vincristine, ifosfamide and actinomycin D in second trimester[51]. One case of fetal myocardial necrosis following third trimester exposure to daunomycin has also been reported[52]. Long-term effects of in-uteroexposure to anticancer drugs on growth, intellectual function, pubertal maturation and reproductive potential needs further data for any relevant conclusions. However, a statistical analysis of the incidence of teratogenecity and malignancies in these children showed no significant increase in comparison to the general population[53]. Most of these cytotoxic drugs get secreted in human breast milk, hence lactation should be suppressed in women who receive chemotherapeutic drugs.

Treatment recommendations depend on the period of gestation, type of malignancy, aggressiveness of the tumour and the stage of disease. Therapeutic abortion should be considered in the first trimester of pregnancy especially in those who are unwilling to accept any increased risk of adverse fetal outcome attributable to therapy. Women who had a teratogenic exposure in the first trimester or who requires treatment immediately because of the aggressive behaviour of the tumour are recommended therapeutic abortion in the first trimester. Chemotherapeutic drugs are avoided in the first trimester especially in the first 8 weeks of gestation. Antimetabolites (especially folic acid antagonists) and procarbazine are better excluded from the chemotherapeutic regimen in pregnancy, especially in the first trimester. Involved field radiation can be contemplated if fetal exposure acceptable, but abdomino pelvic irradiation is contra-indicated at any stage of pregnancy. If possible, therapy can be delayed till delivery, especially in early stage, low grade tumours. But these patients should be under close surveillance for the disease and the status of pregnancy, so that, intervention is not delayed if warranted.

Cancer and pregnancy is a complex clinical problem, success of which is a team approach of oncologist, obstetrician and neonatologist. Inappropriate generalisations must be avoided, though treatment may have to be modified and tailored. Aim should be to kill the cancer, rather than watchful expectancy which can kill the mother and the fetus. However, the value of the compliance of the patient should never be underestimated in taking any therapeutic decision.

Results:

Most of the patients were in the third decade of life (Table 1). 11/13 cases presented in their third trimester of pregnancy. 2 patients who were in the first trimester of pregnancy underwent medical termination of pregnancy before starting the specific treatment. One patient with mixed germ cell tumour of the ovary was diagnosed in the 36th week of the pregnancy. She underwent Ceserean section prior to starting chemotherapy. Another patient was diagnosed as disseminated adeno carcinoma in the 36th week of her pregnancy. She was induced and delivered a normal baby prior to starting chemotherapy. Two cases of acute lymphatic leukemia were given induction chemotherapy with vincristine, doxorubicin, L-asparaginase, prednisolone and intrathecal methotrexate. One patient achieved complete remission and had a normal full term delivery. Baby is doing well, but the mother relapsed and died one and a half years later. Other patient with acute lymphatic leukemia did not achieve remission, but had normal vaginal delivery at 36 weeks. There were 2 patients with acute myeloid leukemia (M2 and M4) diagnosed at 28th and 30th week of their pregnancy. Both of them did not achieve remission with 3/7 chemotherapy with daunorubicin and Ara-C. One of them aborted and the other had intrauterine death of the foetus. Both these patients died within 3 weeks, one with septicemia and the other with intracerebral bleed.

There were two cases of pregnancy associated with choriocarcinoma. Both had chemotherapy with EMACO and delivered normal babies, both being cured of the disease. One case of pregnancy with chronic myeloid leukemia was treated with hydroxyurea and had normal full term delivery.

Squamous cell carcinoma of nasopharynx (T2N2Mx) was diagnosed in the 32nd week of her pregnancy and was treated with chemotherapy. She delivered a normal baby at 37th week. She had radiotherapy to the primary site and nodes later, but was detected to have disseminated bone disease 4 months later. One patient with borderline carcinoma ovary was diagnosed in the 34th week of her pregnancy. She was kept on follow up and delivered a full term normal baby. She underwent pan hysterectomy and staging work up 8 weeks after delivery and both mother and baby are doing fine.

Placenta of all these patients were examined and there was no evidence of placental metastasis in any of these cases.

There were no undue toxicity of chemotherapy in any of these patients except the two cases of acute myeloid leukemia who had uncontrolled protracted vomiting.

Table: 1

Age in years	Diagnosis	Gestation (Wks)	Chemotherapy prior to delivery	Response	Foetus	Mother
28	ALL	34	yes	CR	N	D
27	ALL	32	yes	NR	N	D
20	AML	30	yes	NR	Abortion	D
26	AML	28	yes	NR	IUD	D
25	GTD	30	yes	CR	N	L
22	GTD	32	yes	CR	N	L
24	GCT Ovary	36	No	CR	N	L
24	Disseminated Adenocarcinoma	36	yes	NR	N	D
34	CML	32	yes	SD	N	L
20	Ca Nasopharynx	32	yes	CR	N	D
28	Osteosarcoma	12	No	CR	N	L
26	Borderline Ca Ovary	34	No	CR	N	L
27	NHL	8	No	CR	N	L

GTD - Gestational Trophoblastic disease
GCT ovary-Germ Cell Tumor ovary
NR-No Response
N-Normal
D-Dead

CR- Complete Remission
SD- Stable Disease
IUD- Intra Uterine Death
L-Living

References:

1. Shushan A, Stemmer S.M., Reubinoff B.E., Eid A, Weistein D, Carcinoma of the colon during pregnancu. Obstet Gynaecol Survey 1992; 47: 222-225.
2. Tafuri A. Alfernik J, Moller P, Hammerling G I, Arnold B; t cell awareness of paternal allo antigens during pregnancy. Science 1995; 2170: 630-633.
3. Rojansky N, Shushan A, Livni J, Jurim O, Sulam M and Gabun E., PRegnancy associated with colon carcinoma over expressing P. 53. Gynaecologic Oncology 1997; 64: 516-520.
4. Bearl V, Fraser P, Chilvers C: Does pregnancy protect against ovarian cancer? Lancet, 1978; 1: 1083-1087.
5. Donegan W.L, Cancer and Pregnancy CA 1983; 33: 194-214.
6. Potter J.F, Schoeneman M, Metastasis of maternal cancer to the placenta and fetus. Cancer 1970; 25: 380-388.
7. Rothman L A, Cohen C J, Astarloa J: Placental and fetal involvement by maternal malignancy: A report of rectal carcinoma and review of the literature, Am J obstet Gynecol 1973; 116: 1023-1034.
8. Hass V A; Pregnancy in association with newly diagnosed cancer: A population based epidemiologic assessment. Int. J. Cancer 1984; 34: 229-235.
9. Reintgen D S, Mc Carty K S, Vollmer R. Malignant melanoma and pregnancy. Cancer 1985; 55: 1340-44.
10. Sutherland C M, Loutfei A, Mather F J, Effect of pregnancy upon malignant melanoma. Surg. Gynaecol. Obstet. 1983; 157, 443-446.
11. Haagensen C D, Stout AP; Carcinoma of the breast. Ann Surg 1943; 118: 859-870.
12. George P A, Fortner J G, Pack G.T: Melanoma with pregnancy: Cancer 12960; 13: 854-859.

13. Whhite L P, Linden G, Breslow L; Studies on melanoma. The effect of pregnancy on survival in human melanoma. JAMA 1961; 177: 51-54.
14. Elwood J M, Coldman AJ: Previous pregnancy and melanoma prognosis, Lancet 1978; 2: 1000-1001.
15. Hersey P, Morgan G, Stone DE: Previous pregnancy as a protective factor against death form melanoma. Lancet 1977; 1:.451-452.
16. Shocket E C, Fortner JG: Melanoma an Pregnancy: An experimental evaluation of a clinical impression. Gyn and OB surgical forum, Memorial Sloan Kettering Institute, New York, 1957.
17. Reynoso E E, Shepherd F A, Messner H A. Acute leukemia during pregnancy: The Toronto leukemia study group experience with long term follow up of children exposed in utero to chemotherapeutic agents. J. clin. oncol. 1987; 5: 1098-2106.
18. Mayer R J: Current chemotherapeutic treatment approaches to the management of previously untreated adults with denovo acute myeloblastic leukemia. Semin. oncol. 1987; 14: 384-396.
19. Hoelzer D, Thiel E, Loffler H: Prognostic factors in a multi center study for treatment of acute lymphoblastic leukemia in adults, Blood 1988; 71: 123-131.
20. McLain CR: Leukemia is pregnancy Clin.f Obstet. Gynecol 1974; 17: 185-194.
21. Kardinal CG, Bateman JR, Weiner J: Chronic granulocytic leukemia: Review of 536 cases. Arch intern Med. 1976; 136: 305-313.
22. Barry RM, Diamon HD, Craver LF: Influence of pregnancy on the course of Hodgkins disease. Am. J obstet. Gynecol, 1962; 84: 445-454.
23. Gobbi PG, Attardo-Parrinello G, Danesino M; Hodgkins disease and pregnancy. Haematologica 1984; 69: 336-341.
24. Steiner-Salz D, Yahalom J, Samuelov A; Non Hodgkins lymphoma associated with pregnancy: A report of six cases, with a view of the literature. Cancer 1985; 56: 2087-2091.
25. Ward FT and Weiss RB: Lymphoma and pregnancy. Semin. Oncol 1989; 16: 394-409.
26. Armitage JO, Feagler JR and Skovg DP: Burkitts lymphoma during pregnancy, with bilateral breast involvement. JAMA, 1977; 237: 151.
27. Armon PJ: Burkitt's lumphoma of the ovary in association with pregnancy. Two case reports, Br. J. Obstet., Gynaecol, 1976; 83: 169-172.
28. Bagshawe KD: Treatment of high risk choric carcinoma J. Reprod. MEd 1984; 29: 813-820.
29. Gangadharan VP, Chithrathara K, Satishkumar K, Rajan B, Nair MK: Successful management of chorio carcinoma wiht pregnancy. Acta oncologica 1994; 33(1): 76-77.
30. Eriksson A, Gazelius C: Metastatic chorio carcinoma during normal pregnancy presenting as Thyroid tumour, Arch Gynecol: 1984; 236: 119-22.
31. Beischer N A, Buttery B W, Fortune D W: Growth and malignancy of ovarian tumours in pregnancy. Aust NZ Y Obstet Gynaecol 1971; 11: 208-220.
32. Jolles CJ: Gynaecologic cancer associated with pregnancy; Seminars in oncology, 1989; 16(5): 417-424.
33. Jubb E D: Primary ovarian carcinoma in pregnancy. Am. J Obstet Gynaecol 1963; 85: 345-354.
34. Sweet DL: Malignant lymphoma: Implications during the reproductive years and pregnancy. J Reprod. Med. 1976; 17: 198-208.
35. Cases B W, Benaroya S: Dyspnea in a pregnant young woman. Can Med. Asso. J. 1980; 122: 890-896.
36. Ortega J: Multiple agent chemotherapy including bleomycin of non-Hodgkins lymphoma during pregnancy. Cancer 1977; 40: 2829-2835.
37. Grag A, Kochupillai V; Non-Hodgkins lymphoma in pregnancy. South Med. J. 1985; 78: 1263-1264.
38. Goldwasser F, Pico JL, Cerrina J, Fernandez J, Pons J C, Cosset J M and Hayat M: Successful chemotherapy including Epirubicin in a pregnant non-hodgkins lymphoma patient. Leukemdia and lymnphoma 1995; 20: 173-176.
39. White K C; Ovarian tumour in pregnancy. Am J Obstet Gynecol 1973; 116: 544-550.
40. Buttery B W, Beischer NA, Firtybe D W: Ovarian tumours pregnancy. Med. J. Aust 1973; 1: 345-349.
41. Mole R H: Radiation effects on prenatal development and their radiological significance Br. J. Radiol, 1979; 52: 89-101.
42. Hammer-Jacobson E: Therapeutic abortion on account of X-ray examination during pregnancy. Dan. Med. Bull 1959; 6: 122.
43. Blatt J, Mulvihill J J, Ziegler J L, Young R C and Poplack D G: Pregnancy outcome following cancer chemotherapy. Am J Med. 1980; 69: 828-832.
44. Gililland J and Wernstein L: The effect of cancer chemotherapeutic agents on the developing fetus. Obstet. Gynecol. Surg. 1983; 38: 613.
45. Dealvarez R R: An evaluation of Aminopterin as an abortifacient. Am. J. Obstet. Gynecol 1962; 83: 1467-1477.
46. Panchalingham S: Post-methotrexate babies. Ceylon Med.,J. 1973; 18: 93-97.
47. Nicholson H D: Cytotoxic drugs in pregnancy. J. Obstet. Gynecol. Brit. Gwith 1968; 75: 307-312.
48. Sutcliffe S B: Treatment of neoplastic disease during pregnancy: Maternal and fetal effects. Clin. Invest. Med. 1985; 8: 333-338.
49. Okum D B, Groncy PK, Sieger L and Tanaka KR: Acute leukemia in pregnancy. Transient neonatal myelosuppression after combination chemotherapy in the mother. Med. Ped. Oncol. 1979; 7: 315-319.
50. Raffles A, Williams J< Costeloe K and Clark P: Transplacental effects of maternal cancer chemotherapy. Case report. Br. J. Obst. Gynecol 1989; 96: 1099-1100.
51. Fernandez H, Diallo A, Bauma D and Papiernik E. Anhydramnios and cessation of fetal growth in a pregnant mother with poly chemotherapy during the secxond trimester. Pren. Diagnosis 1989; 9: 681-682.
52. Schaison G, Jacquillat C, Aucleore G, Weil M, Les fisques foeto-emryonnainess des chimiotherapies Bull. Cancer 1979; 66: 165-170.
53. Mulvihill J J, Mckeen E A, Rosner F and Zarrbi M H; Pregnancy outcome in cancer patients. Cancer 1987; 60: 1143-1150.

HISTOPATHOLOGICAL STUDY OF CHRONIC CALCIFYING PANCREATITIS (CCP) From Kashmir Valley

Azra Shah M.D.

Abstract: Open surgical biopsies of 16 patients of chronic calcifying pancreatitis were studied over an eight year period. There were four males and twelve females with the mean age at presentation 35.4 years. The significant features on histology were patchylobular distribution of lesions, irregular dilatation of ducts, presence of calcified stones in only 37.5% cases and chronic inflammatory infiltrates in the intrapancreatic nerve fibres. Four cases had associated pancreatic adenocarcinoma.

Key words: Chronic Pancreatitis, Calcification.

JK-Practitioner 1999; (6)2: 130-131

Introduction

Chronic calcifying pancreatitis (CCP) is a distinct disease entity chracterised by the formation of intraacinar and intraductal precipitates in the early stages of the disease and calculi in the advanced stages[1-3]. The calculi are built up of two different components: insoluble calcium salts and various degraded and insoluble residues of a secretory protein (lithostatine S[3]). CCP of unknown cause, not related to alcohol intake is prevalent in India and Africa in an epidemic form. The most typical form of the disease has been described from Kerala, South India[4]. The mean age at clinical onset of the disease is 12.5 years[5].

The purpose of this paper is to present our experience of the histopathology of 16 cases of CCP from Kashmir and its association with pancreatic adenocarcinoma.

Material and Methods

Open surgical biopsies of 16 patients with a clinicoradiological diagnosis of CCP were studied over an eight year period in the department of Pathology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar. The biopsies were fixed in 10% buffered formalin and stained by the Haematoxylin and Eosin stain. Special stains like PAS-Alcian blue at pH2.5 (for acid and neutral mucins), Masson's trichome (for fibrous tissue) and Von Kossa stain (for calcium) were performed wherever necessary.

Results

The study included 16 patients, 4 males and 12 females, with a male to female ratio of 1:3. The age ranged between 20 and 55 years. The mean age at presentation was 35.6 years.

Histology

The histology was characterised by irregular, patchy, lobular distribution of the lesions. There was dense fibrosis of the parenchyma with loss of acinar and islet cell tissue in all cases. Occasional duct showed ulceration or squamous metaplasia of the lining epithelium. Periductal fibrosis deforming the ducts and causing angulations was seen in 10 cases (62.5%) (Fig.1). The intervening parenchyma showed focal to diffuse infiltration by chronic inflammatory cells especially lymphocytes, plasma cells and histiocytes. Scattered lymphoid nodules were present in 8(50%) cases and marked acinar atrophy with perilobular and intralobular sclerosis in 12 (75%) cases. Four cases (25%) had microscopic calcification in the

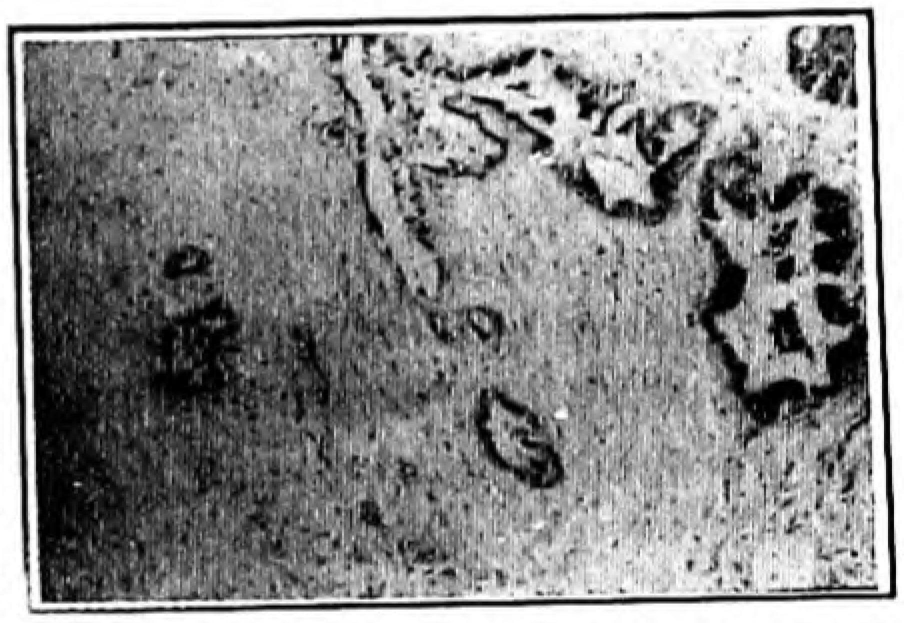


Fig.I: Photomicrograph showing acimaratrphy, dense fibrosis of paranchyma periductal fibrosis and angulations of the ducts (HXEx100)

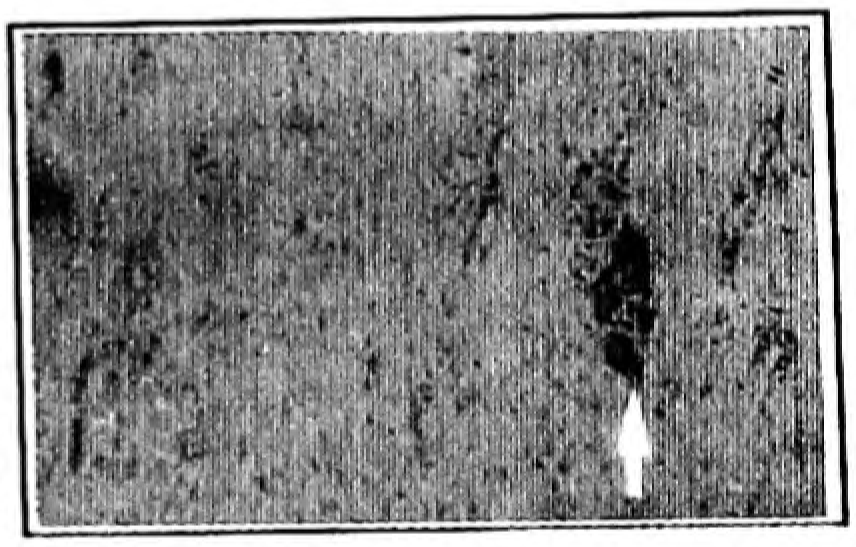


Fig.II: Photomicrograph showing acinar destruction and infracinar calcification (HXEx100)

From the Department of Pathology, SKIMS, Soura, Srinagar, India (Prof. Azra)

Received November 1998 Accepted Febuary 1999

Corespondence: Prof. Azra Shah, Head of Department of Pathology, SKIMS, Soura, Srinagar P.O.Box No. 27, Kashmir, India.

pancreatic parenchyma (Fig.2) and 2 cases (12.5%) had greyish-white intraductal calculi. Protein precipitates in the duct lumina were seen though not very prominent.

A perineural inflammatory cell infiltrate of lymphocytes and plasma cells within the intrapancreatic nerve fibres was a striking feature. Normal islets were scattered focally, though decreased in number.

Association with pancreatic carcinoma:

Four patients (25%) had pancreatic carcinoma on surgery. None of the cases had pre-operative diagnosis of malignancy nor was it picked up on ultrasound and/ or ERCP. The indications of surgery in these four cases were intractable abdominal pain in three patients and progressive extrahepatic cholestasis in one patient.

Discussion

Tropical CCP was first reported from Kerala, South India where the disease in endemic and occurs in 5.4% of the general autopsy population and 1-1.5% of hospital admissions[6-8]. It has also been reported from Mumbai[9] and Chennai[10]. This report is the first description of the histomorphology of CCP from Kashmir to the best of our knowledge.

In this study the majority of cases were adults which is similar to the results published in studies from Europe[11,12], but is markedly different from the classical presentation of tropical CCP described from South India where the mean onset of disease is 12.5 years[5]. The disease was more common in females with the female: male ratio 3:1. The significant features of the disease on histology were (1) a patchy lobular distribution of the lesions. This is in contrast to the regular distribution of lesions observed in chronic obstructive pancreatitis, (2) frequency of duct lesions with irregular dilatation, (3) presence of eosinophilic protein plugs or calcified stones in only 37.5% cases in comparison with the frequency of these in other studies, (4) lesions of intrapancreatic nerve fibres with perineural inflammatory infiltrates. Four cases had associated pancreatic adenocarcinoma. Although CCP is not recognized as a major risk factor for pancreatic carcinoma[14], chronic irritation and metaplasia by stones in the ducts eventually lead to carcinoma.

There are different views regarding the pathogenesis of CCP. It is considered not to be a primary inflammatory disease of the pancreas but a lithiasis[15]. The protein precipitates and stones are responsible for atrophy and disappearance of duct epithelium-causing multiple strictures of the pancreatic duct. The other lesions are secondary to obstruction by protein plugs, stones and strictures.

Presence of lymphocytes with formation of lymphoid follicles and infiltration by mononuclears within nerve fibres may point towards an immunologic mechanism for CCP, the immune mechanisms may play a role in the destruction of previously diseased cells[16]

References:

1. Payan H, Sarles H, Demirdjian M, Gauthier AP, Cros RC, Durbee JP. Study of histological features of chronic pancreatitis by correspondence analysis -Identification of CCP as an entity. Biomedicine 1973; 18: 663-670.
2. Tasso F, Stemmelin N, Sarles H, Clop J. Comparative morphometric study of the human pancreas in its normal state and in primary CCP. Biomedicine 1973; 18: 134-144.
3. Sarles H, Bernard JP, Johnson C. Pathogenesis and epidemiology of chronic pancreatitis. Amer Rev Med 1989; 40: 453-477.
4. Narendranathan M. CCP of the tropics. Tropical Gastroenterology 1981; 2: 40-45.
5. Sarles H. An international survey on nutrition and pancreatitis. Digestion 1973; 9: 389-403.
6. Mokolo C, Dil J. Pathogenesis of juvenile tropical pancreatitis syndrome. Lancet 1980; 1: 456-458.
7. Geeverghese PJ, Pillai VK, Joseph MP, Pitchumoni CS. The diagnosis of pancreatogeneous diabetes mellitus. J Ass Phys India 1962; 10: 173-180.
8. Sarles H. Chronic calcifying pancreatitis -chronic alcholic pancreatitis. Gastroenterology 1974; 66: 604-616.
9. Geeverghese PJ. Pancreatic diabetes - A clinicopathologic study of growth onset diabetes with pancreatic calculi. Bombay Popular Prakashan 1968.
10. Vishwanathan M, Sampath KS, Subhramanyam S, Krishnaswami CV. Etiopathogenesis and clinical angle of pancreatic diabetes mellitus from Madras. J Ass PJhys India 1973; 21: 752-759.
11. Sarles H, Cros RC, Bidart JM. International group study of pancreatic disease - A multicenter enquiry into the etiology of pancreatic diseases. Digestion 111979; 19: 110-125.
12. Sarles H, Camarena J, Gomez-Santana C. Radiolucent and calcified pancreatic lithiasis, two different diseases - Role of alcohol and heredity. Scand J Gastroenterol 1992; 27: 71-76.
13. Sarles H, Laugier R, Eoustieres C. Pancreatic lithiasis, alcoholic pancreatitis, pancreatitis, pathogenesis - In progress in Gastroenterology. Eds. Jerzy Glass and Sherlock P. Grune and Stratton NY 1983; 4: 189-2112.
14. Abrahim PA. Pancreatic lithiasis. Ind J Surg 1969; 31: 588-596.
15. Edmondson HA, Bullock WK, Mahi JW. Chronic pancreatitis and lithiasis - pathology and pathogenesis of pancreatic lithiasis. Amer J path 1984; 26: 37-44.
16. Dani R, Antines LJ, Ribeiro JEF, Nogueira CED, and Ribeiro T. Immunological participation in CCP. Digestion 1974; 11: 333-337.

PRIMARY PARATESTICULAR MALIGNANCY-HISTOPATHOLOGICAL STUDY

A.R. Khan M.D.; N.D. Chowdhary M.D.

Abstract: 3 cases of embryonal rhabdomyosarcoma in children aged 5,6 and 14 years and 2 cases of leiomyosarcoma, in 60 and 68 year old men from surgical pathology over 14 years period 1984-97. All presented with scrotal swelling. Tumor deposits were seen in iliac and retroperitoneal nodes in a case, each from the rhabdomyosarcoma and leiomyosarcoma respectively.

Key words: Paratesticular sarcoma, Rhabdomyo-sarcoma, Leiomyo-sarcoma.

JK-Practitioner 1999; 6(2): 132-134

Introduction

Primary paratesticular malignancy is rare. The most common malignancy reported in children is the rhabdomyosarcoma, and the paratesticular region is the most common site, seen predominantly in the age group 7-18 years[1]. Liposarcoma is the most common primary malignancy of the adults in this region followed by leiomyosarcoma[2]. The literature reviews only case reports[3,4,5,6,7 & 8]

Material and Methods

The study comprises of retrospective and prospective analysis of paratesticular tumors over a 14 year period. The table 1 summarises the list of tumor encountered. The report however, discusses only the primary malignancies.

The material comprises of surgical material from pathology Department Medical College and referal clinic. The specimen slides and blocks were utilised for the study. In addition to hematoxylin and eosin, other histochemical stains used were Periodic Acid Schiff/ Alcian blue, Reticulin and Phosphotungstic acid hematoxylin.

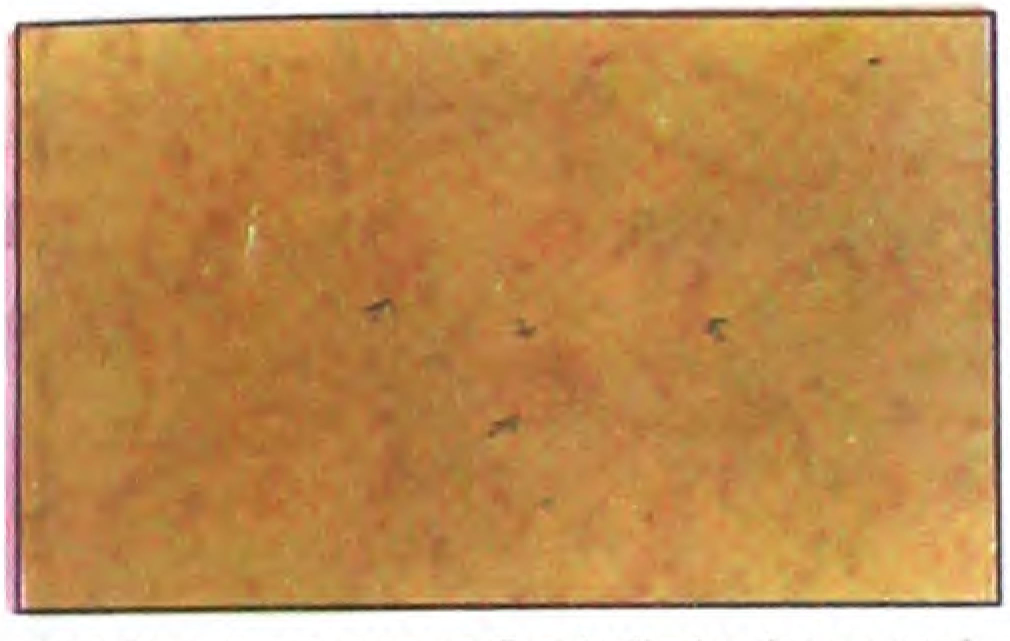


Fig.I. Rhabdomyo sarcoma-Paratesticular shows round and spindle cells with rhabdomyoblasts (arrow). HxEx400.

Observation

As seen in the table 2, three cases of rhabdomyosacroma were seen in boys aged 5,6,14 years. All presented with scrotal masses of 3-6 months duration. This includes one case (case No. 3) where only review slides were available. External iliac nodes were enlarged in one case (case No. 2), the two cases of leiomyosarcoma occured in men aged 60 and 68 years. Both presented with the scrotal masses. The scrotal mass in one case (case No. 5) was very massive. This patient had also extensive involvement of retroperitoneal lymph nodes and died 2 months later.

Pathology

Gross findings as shown in the table 2, the maximum diameter of 2 cases of rhabdomyosarcoma was 30 mm and 35 mm. The tumors were well circumscribed, in the region of epididymis and spermatic cord. Cut surface revealed greyish soft to firm tumors. Testis was well delineated and free of tumor infiltration. The two leiomyosarcoma measured 80 mm and 140 mm in longest dimensions, with compression atrophy of testis, which could be identified grossly only in case No. 4

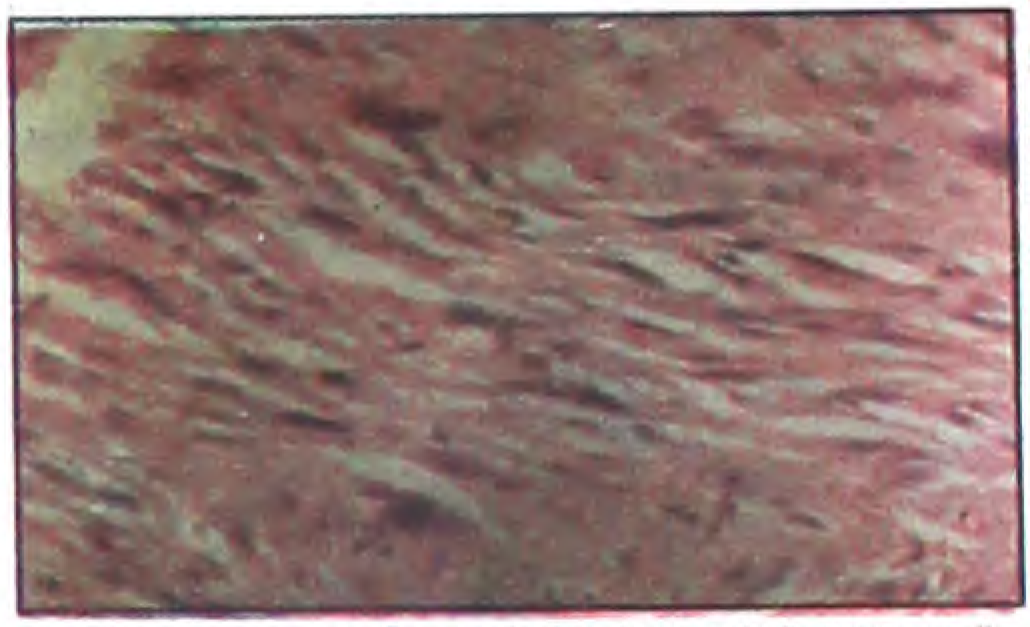


Fig.II. Leiomyosarcoma-Paratesticular shows spindle tumour cells with moderate nuclear pleomorphisim HxEx400.

The microscopy of cases 1,2 and 3 showed typical morphology of embryonal rhabdom yosracoma. There were typical spindle and polygonal tumor cells with hyperchromatic nuclei and scanty pale toeosinoph-ilic cytoplam as well as larger roundish and elongated tumor cells with abundant cytoplasm with cross striations. Many mitotic divisions were present. The stroma was scanty loose myxoid. The two cases of leiomyosarcoma were well differentiated with interlacing spindle cells

From the Department of Pathology Govt. Medical College Srinagar Kashmir (Khan, Chowdhary)

Received July 1998 Accepted February 1999

Correspondence to: Prof. A.R. Khan, Deptt. of Pathology GMC, Srinagar, Kashmir, India.

With Best Compliments From:

CAULSON & CO

IST BRIDGE, SRINAGAR, KASHMIR; TEL. (O) 472145 (R) 474355

We Stock & Service
Littmann Stethoscopes

Authorised Dealers of:

Johnson & Johson Ltd.
Ethicon, Hospital Products & Ortho Divisions.

Birla 3M Ltd.

Stryker Products
(Div. of Nicholas Piramal India Ltd.)

Laparoscopic, Arthroscopic &
Sinuascopic Equipments.

Equipments for all Types of Orthopeadic,
Neurological & Spinal Surgeries.

having fibrillar eosinophilic cytoplasm and vesicular nuclei. The mitotic figures could easily be spotted. The retroperitoneal mass was confirmed as metastatic deposits of leiomyosarcoma by fine needle aspiration cytology.

Discussion

Malignant paratesticular tumors can arise from the testicular tunica, epididymis and spermatic cord. The paratesticular, region is the most common site of embryonal rhabdomyosarcoma, seen in children and adolescence, predominantly in patients between 7 and 18 years of age[2]. The tumors are invariably of embryonal type and rarely of spindle cell morphology.

The genesis of the rhabdomyosarcoma is thought to be either displacement of myotoma tissue along the ductus deferens or displacement of the primitive mesenchymal precussors along the areas of the existing skeletal muscle mass[6,7] The diagnosis is histologic.

Prognosis of the tumors was dismal before introduction of multidisciplinary approach, has changed dramatically with a 5 years survival of 80 to 90 percent in histologically favourable type[9]. The intergroup rhabdomyosarcoma study revealed a 40 percent incidence of retroperitoneal node compared to a 15 percent of histologically demonstrable venous invasion in paratesticular rhabdomyosarcoma[10]

Table-I
Paratesticular neoplasm

	Malignant neoplasmas	No of cases
A.	Malignant primary	
	1. Rhabdomyosarcoma	3
	2. Leiomyosarcoma	2
	Total	5
B.	Secondary	
	a. Spread from testis	
	1. Seminoma	2
	2. Non-Hodgkin's lymphoma	2
	3. Hodgkin's Disease	1
	Total	5
	b. Systemic dissemination	
	1. Non-Hodgkin's lymphoma	2
	2 Seminoma	2
	3 Metastatic adeno-carcinoma	2
	Total	6
II.	Benign neoplasms	
	1. Adenomatoid tumor	4
	2. Adenomatoid tumor with leiomyoma	1
	3. Leiomyoma	1
	4. Fibroma	1
	5. Lipoma	1
	6. Cystadenoma	1
	Total	9

The most common primary testicular malignancy in adults reported is liposarcoma, followed by leiomyosarcoma, fibrosarcoma, malignant mesotheliomas and adeno carcinoma of epidydimis[2]. We have come across only two cases of leiomyosarcoma over 14 years period. Bolla and Arkell[11] while reporting a case of leiomyosarcoma of the spermatic cord collected 32 cases from the literature since its first description by Patel in 1907. Till recently more than 100 cases have been reported.[2]. More than 80 percent of patients are seen over the age of 40 years. They usually present with scrotal mass of variable size and duration with or without metastasis.

Table II
Primary Malignant Paratesticular Tumors

S.No.	Age (years)	Side	Maximum (diameter)	Matastasis	Histology
1.	14	R	35mm		Embryonal rhabdomyosarcoma
2	5	L	30mm	Iliac lymph	
3.	6	Only slides reviewed			Embryonal rhabdomyosarcoma
4.	60M	L	80mm		Leiomyosarcoma
5.	68M	R	140mm	Retroperitoneal nodes	Leiomyosarcoma

Tumors arise more often from the spermatic cord than the epidydimis[12]. However the exact site of origin is difficult to determine in the advanced cases. The behaviour of the tumor varies with the size and tumor grade. Both local recurrences and metastasis occur depending on the adequacy of the excision and stage of the disease. The tumor spreads by lymphatics as well as through blood. Extensive retroperitoneal metastatic deposits were seen in one of our cases (case No. 5) who died 2 months after the diagnosis. Diagnosis is histopathologic. Whereas there is no problem in diagnosing well differentiated and pleomorphic types, the borderline cases, pose a challange and need differentiation from leiomyoma, a more commoner tumor in the region. The mitotic count of 1-2 per high power field as suggested by Mostofi and Price[13] is supposed to be helpful. Such cases would demand simple excision with clear margins followed by careful follow up.

References:

1. Enzinger FM Weiss SW. In soft tissue tumours 1988, II Edition p 451. Ed Enzinger FM Weiss SW. The C.V. Mosby Company.
2. Bostwich DG. In Urologic Surg Path p 663, 1997 Ed. Bostwich DG and Eble JN Mosby.
3. Abell MH, Holtz F. Testicular and paratesticular noplasms in patients 60 years of age and older. Cancer 1967;5: 852.
4. Rosas-uribe A Luna MA Guinn GA. Paratesticular rhabdomyosarcoma. A clinicopathologic study of seven cases. The Am J of Surg 1970; 120: 787.
5. Chitale A. Vadera A. Neoplasms of testis and paratesticular

tissues, in Pathology of urinary and male genital system 1992, p 226. Ed Chital A Vadera A. B.I. Churchil livingstone.

6. Arean VM Kreager JA. Paratesticular rhabdomyosarcoma. Am J Clin Path 1965; 43: 418.
7. Gray CP Biorm CL. Myosarcoma of the spermatic cord. J Urol 1960.
8. Banik S Guha PK Paratesticular rhabdomyosarcoma in leiomyosarcoma. A clinicopathologic review J Urol 1979; 121: 823.
9. Rodary C Geham EA Flamant F et al. Prognostic factors in non- metastatic rhabdomyosarcoma in children. A report from the International Rhabdomysoarcoma Workship Med Pediatr. Oncol 1991; 19: 89.
10. Raney RB Jr Hays Lawrence W Jr. et al. Paratesticular rhabdomyesarcoma in childhood. Cancer 1978; 42: 729.
11. de Bolla AR Arkell DG. Leiomyosarcoma of the spermatic cord. Post gard Med J 1983; 59: 470.
12. Helm RH Al-Tikriti S. Primary leiomyosarcoma of the epidydimis. Br. J Urol 1986; 58: 99.
13. Mostofi FK Price EBJ. Tumors of the male genital system. Atlas of tumor pathology, fascicle 8/, 2nd series Washington DC 1973. Armed Forces Institute of Pathology.

With Best Compliments From

SUPREME SYNDICATE

Complete Hospital and Laboratory Furnishers and
Pharmaceutical Distributors

267, NURSING GARH, SRINAGAR-190 001 (KASHMIR) PHONES : 471528, 478712; FAX : 0194-430645

AUTHORISED STOCKISTS FOR:

CHEMICALS:

E.Merck (I) Ltd.
B.D.H. Chemicls
S.D.Fine Chem. Ltd.
Hi-Media Laboratories

GLASS WARE:

Durani (German) Glass Ware
Blue Star Glass Slides & Cover Slips

EQUIPMENTS:

Getner Microscopes
Suvira Audio Visual Equipments
Sipcon Microtones/Tissue Processors
Jindal Lab. Equipments

SOME EPIDEMIOLOGICAL FEATURES OF HYPERTENSION IN RURAL KASHMIRIS

Wani Yasmeen, M.D.; Imtiyaz Ali, M.D.; Bhat Nazir Ahmad, M.D.

Abstract: *The present study was carried out in Ganderbal Block (rural area), covering 1560 persons (both males and females) above 20 years of age. The study was of cross-sectional design and prevalence rate of 15.38% hypertension among rural subjects was observed being more in females (20.86%) than in males (10.40%). Age, sex, smoking, family income, literacy status, occupation, family history of hypertension and obesity have been found to have their significant association ($p<0.001$) with prevalence of hypertension. The risk of hypertension in association with various sociomedical factors is discussed.*

Key words: *Hypertension, Prevalence, Age, Sex, Socioeconomic status, Smoking and Obesity.*

JK-Practitioner 1999; 6(2): 135-138

Introduction

Hypertension has assumed significance because of being a major public health problem all over the world, both in developed and developing countries. It affects 8 to 18% of world's adult population. During recent years an increasing trend in the incidence of hypertension has been observed all over the world especially in developing countries (WHO, 1978)[1]. It is unlikely that a single factor is responsible and therefore, currently a multifactorial approach is favoured (Scotch, 1963)[2]. The actual causative factors having their direct impact on the course of etiopathogenesis of hypertension still remains a challenge. The design and planning of present study aims to identify some epidemiological features having their direct or indirect bearing on hypertension in a rural set up.

Material and Methods

A cross-sectional survey in Block Ganderbal which is field practice area of Social & Preventive Medicine Department Government Medical College, Srinagar was conducted to find out prevalence of hypertension in both sexes above 20 years of age. A total of five villages selected randomly were taken from different sectors of Ganderbal. A house to house survey was conducted and population above 20 years of age was enumerated and enlisted. Absenties were contacted in subsequent visits. All subjects were apprised of the aim of the study. To obtain information pertaining to socio-economic status of the families the total monthly income, literacy level and occupation of subject were recorded on a pre-designed proforma. Addiction if any and family history of hypertension was also recorded. All the individuals were subjected to detailed general physical and systemic examination to exclude any systemic disease. Blood pressure and anthropometric measurements were recorded as given below:

Blood Pressure:

Blood pressure was recorded by using standard indirect auscultatory method as described by Karotkoff (Best & Tylor, 1973)[3]. Average of two reading was taken. The criteria for labelling a person as hypertensive was same as used by the W.H.O definition of hypertension (WHO 1978)[1]. According to which hypertension is a chronically elevated systolic and/or diastolic blood pressure with following levels:

Borderline hypertension: Blood pressure greater than 140/90 mmHg, but less than 160/95 mmHg.

Established hypertension: Blood pressure greater than or equal to 160/95 mmHg.

Blood pressure levels upto 140/90 mmHg are taken as normal in adults.

Height and Weight:

Height and weight measurements were taken in accordance with standard methods prescribed by Jelliffe and Jelliffe (1966)[4]. Height in centimeters was measured by vertical scale in upright position to the nearest of half a centimeter after removing shoes. Weight in kilograms with minimum clothing and without shoes was recorded to the nearest of quarter of kilogram on a portable

From the Department of Community Medicine SKIMS, Soura, Srinagar (Yasmeen, Ali, Bhat)

Received August 1998 Accepted March 1999

Correspondence to : Dr. Imtiyaz Ali, Prof. & Head Deptt. of Community Medicine, SKIMS, Soura, Srinagar-190011, Kashmir GPO Post Box No. 27

weighing machine.

For estimating obesity Brocas Index was applied according to which height in centimeters minus 100 gives ideal weight in Kg. Those above this weight are considered Obese (Park 1986)[5].

The data has been subjected to Chi-square test for drawing inferences and conclusions.

Observations

The overall prevalence of hypertension in Block Ganderbal was found to be 15.38% in both the sexes (Table-I). Maximum prevalence of the order of 42% was seen in the age group of 65-69 years and almost a similar frequency (40.82%) in the age group of 70 years and above. The average prevalence of hypertension below the age of 50 years and above the age of 50 years was 9.35% and 31.4% respectively. This difference was highly significant ($p<.001$). Of the total 240hypertensive cases 155(20.86%) were females and 85(10.40%) were males (Table-2). The difference in prevalence of hypertension by sex was statistically highly significant at $p<.001$.

Table-1

Prevalence of hypertension among both sexes combined

Age in Years	Total persons studied	No. of hypertensive cases	Prevalence percentage
20-24	182	4	2.20
25-29	207	9	4.35
30-34	225	13	5.78
35-39	209	19	9.09
40-44	176	26	14.77
45-49	135	35	25.93
	1134	106(9.35%)	
50-54	122	36	29.51
55-59	120	32	26.67
60-64	85	25	29.41
65-69	50	21	42.00
70 & above	49	20	40.82
	426	134(31.46%)	
All ages	1560	240	15.38

Remarks: $X^2 = 116.26$, $p<.001$ Highly significant.

Table-2

Sex-wise distribution of hypertension cases

Sex	Total persons screened	No. of cases	%age	Remarks
Males	817	85	10.40	$X^2=32.67$
Females	743	155	20.86	$p<.001$ Highly significant
Total	1560	240	15.38	

Table-3 shows that a sizable proportion i.e. 49.9% (779 out of 1560) of subjects were found to be habitual smokers. The prevalence of hypertenison among smokers was found to be very high (24.13%) than in non-smokers (6.66%) and difference of prevalence of hypertension among two groups was found to be highly significant at $p<.001$.

Table-3

Distribution of cases in relation to smoking

Smoking	Total persons	Total hypertensive cases No.	percentage
Present	779	188	24.13
Absent	781	52	6.66
Total	1560	240	15.38

Remakrs: $X^2=91.49$, $p<.001$ HIghly significant.

Table-4

Association of hypertension with family income

Family income in rupees	Total person	Total hypertension cases No.	percentage
<500	329	32	9.73
500-1000	105	12	11.43
1000-1500	1096	187	17.06
1500 & above	30	9	30.00
Total	1560	240	25.38

Remarks: $X^2=16.64$, $p<.001$ Highly significant

The families were categorized into four groups on the basis of average monthly income and studied in relation to hypertension and showed (Table-4). That highest prevalence (30.00%) of hypetension was among those with average monthly family income of Rs. 1500/- and above. Those with monthly income of Rs. 100-1500, Rs. 500-1000 and below Rs. 500- revealed a prevalence rate of 17.06%, 11.43% and 9.73% respectively. The difference in prevalence of hypertension between various economic groups was found highly significant at $p<.001$.

Out of total 1560 cases 1099 (70.45%) were found to be illiterate and out of 240 hypertensive cases (Table-5) maximum number 197 (17.93%) were found in this group and minimum number 43(9.33%) of hypertensives were literate. The preponderance of hypertensives among illiterates was significant at $p<.001$. Table-6 shows that majority of cases i.e. 1181 (75.70%) were farmers and only 33(2.11%) were businessmen. The prevalence of hypertension among businessmen was 36.36% followed by 28.70% in government servants and slightly lower among farmers, skilled and unskilled labours being 14.56%, 12.70% and 10.97% respectively. The association of hypertension with occupation was highly significant at $p<.001$.

Table-5

Distribution of cases in relation to literacy.

Literacy status	Total persons	Total hypertensive cases	
		No.	percentage
Illiterate	1099	197	17.93
Literate	461	43	9.33
Total	1560	140	15.38

Remarks: X^2= 18.44, p<.001 Highly significant.

Table-6

Distribution of cases with occupation.

Occupation	Total persons	Total hypertensive cases	
		No.	percentage
Farmers	1181	172	14.56
Govt. servants	101	31	28.70
Business men	33	12	36.36
Skilled labour	63	8	12.70
Unskilled labour	155	17	10.97
Others	20	-	-
Total	1560	240	15.38

Remarks: X^2= 28.83, p<.001 Highly significant.

Out of 355 cases with positive family history of hypertension, 128 (36.06%) were observed to be hypertensive (Table-7) compared to only 9.29% (112 out of 1205) among those without family history of hypertension. The difference between two groups was highly significant at p<0.001.

While analyzing the effect of obesity on hypertension (Table-8) it was observed that out of 24 over weight males 62.50% (15 subjects) were hypertensive in comparison to only 8.83% with normal weight. The difference in two groups being significant at p<.001. Similarly prevalence of hypertension in overweight females was seen to be 84.29% in contrast to 14.26% in females with normal weight. The difference being highly significant at p<0.001. Total cases of hypertensives (both males and females) among obese were 78.72%, as compared to only 11.32%, among non-obese persons. The difference among two groups being highly significant at p<.001.

Table-8

Relationship of body weight with hypertension

	Males		Females		Both sexes	
Body weight	Total	Hypten. No. (%)	Total	Hypten. No. (%)	Total	Hypten. No. (%)
Over weight	24	15(62.50)	70	59(84.29)	94	74(78.72)
Normal weight	793	70(8.83)	673	96(14.26)	1466	166(11.32)
Total	817	85(10.40)	743	155(20.86)	1560	240(15.38)
Remarks:	X^2=71.88 p<.001 Highly significantly		X^2= 188.34 p<.001 Highly significantly		X^2= 308.31 p<.001 Highly significantly	

Table-7

Distribution of cases as per family history

Family history of hypertensives	Total persons studies	Total hypertensive cases	
		No.	Percentage
Present	355	128	36.06
Absent	1205	112	9.29
Total	1560	240	15.38

Remarks: X^2= 150.84, p<.001 Highly significant.

Discussion

The overall prevalence of 15.28% in both sexes with 10.40% among males and 20.86% among females seen in present study is in consisten with Malhotra (1970)[6] and Gupta et al (1978)[7] who reported similar high rates of hypertension of 15.2% and 13.45% respectively. Tseng (1967)[8] reported higher rates among females than in males being 10.5% to 17% among males and 12.2% to 20.2% among females. Stavig et al (1984)[9] has also reported higher prevalence of hypertension among females than in males after 50 years of age in California. The reason for higher rates among females could be due to the fact that women are more obese than men and subjected to less physical activity than men. Only 2.93% (24 out of 817) males were obese as compared to 9.42% females (70 out 743). Even preponderance of hypertension was more among obese males and females (62.50% and 84.29%) as compared with non-obese males and females (8.83% and 14.26%). Earlier studies conducted by Indrayan et al (1974)[10] and Rao et al (1984)[11] has also shown similar results. The argument may be attributed to hypercholesterolaemia which is associated with obesity and hypertension. Our study also shows rise of blood pressure with age. Maximum prevalence (42%) being in the age group of 65 years onwards. The average prevalence below the age of 50 yearrs was 9.35% and above 50 years was 31.46%. A similar trend of increase in blood pressure with age was also reported by Tseng (1967)[8] and Staving (1984)[9]. The increase in blood pressure in older age is associated with arteriosclerosis. Hypertension had a strong association with smoking in our study, where 24.13% hypertensives were smokers in contrast to only 6.66% cases among non-smokers. The finding is in agreement with Carel et al (1984)[12] and Fouriaud et al (1984)[13]. Tobacco and cigaratte contain nicotine which stimulates post ganglionic neurons which causes vasoconstriction and rise of blood pressure. Nicotine also stimulates A.D.H release which leads to hypertension (Harrison 1983)[14]. Higher income group had a higher prevalence of hypertension (30%) than the lower income group (9.73%) and findings being in conformity with Malhotra (1979)[6] and Rao et al (1984)[11]. It appears that in higher income group it is the life style and dietary factors which contrbute to hypertension. They suffer from more stress and strains of life than poor. More over low physical activity and high caloric diet among rich is likely to lead to obesity and hypertension. Effect of education showing inverse relationship with hypertension being higher in illiterates (17.93%) as compared to literates (9.33%). Similar findings have also been upheld by Fouriaud et al (1984)[13] and Stavig et al (1984)[9]. Role of education is self explanatory, because educated class is more health conscious and takes preventive measures to protect their health. Occupation wise analysis showing higher prevalence of hypertension among businessmen (36.36%) and government servants (28.70%) as compared to farmers, skilled and unskilled labourers, who had prevalence rates of 14.56%, 12.70% and 10.97% respectively. It can be explained on the basis that type of occupation mainly through amount of physical activity and life style influences mechanism which act as risk factor in hypertension. Family history of hypertension had direct association with hypertension. It was found that 36.06% were among those who had family history of hypertension in contrast of 9.29% cases who had not. Similar results were observed by Tseng (1967)[13]. It shows that genetic factors also play part in hypertension.

Conclusion

To conclude, control of hypertension in a community will need study of locally active risk factors to identify most important factor with higher relative risk which can be manipulated to reduce the hypertension in a particular community. The approach will always remain multifactoral one.

References:

1. W.H.O. T.R.S. Arterial hypertension 628, 1978.
2. Scotch NA. Socio-cultural factors in epidemiology of Zulu Hypertension. Am J Public Health and National Health 1963; 53: 1205-13.
3. Best, and Tylor. Physiological basis of medical practice. 3-148, 9th Edition, 1973.
4. JelliffDB. The assessment of nutrition of community. W.H.O Geneva: 1966; 64: 64-67.
5. Park JE and Park T. Assessment of obesity (Brocas Index). Textbook of Preventive and Social Medicine, 10 edition 384, 1985.
6. Malhotra SL. Dietary factors causing hypertension. Am J Clinical Nut 1970; 22(10): 1553-65.
7. Gupta SP, Siwachi SB, Moda UK. Epidemiology of hypertension based on total community survey in an urban population (Rohtak). Ind Heart J 1978; 30(6): 315.
8. Tseng WP. Blood pressure and hypertension in an agricultural and fishing population. Am J Epidemiol 1967; 86(3): 513-25.
9. Stavig GR, Igra A, Leonard AR. Hypertension among Asians and Pacific Islanders in California Am J Epidemiol 1984; 119(5): 677-90.
10. Indrayan A, Kumar A, Srivastava RN. Multifactorial analysis of blood pressure level in Allahabad Urban Community. Ind Jr Public Health 1974; 18(1): 3-7.
11. Rao PSS, Inbaraj SGf, Subramunium VR. Blood pressure measure among women in South Indians. J Epi & Community health 1984; 38: 49-53.
12. Carel RS, Shoenfeld YJ, Elder M, Silverberg DS, Elder Z, Pinkar J, More G. Casual blood pressure, its relationship to Cardio Vascular disease risk factor in middle aged men. J Public Health 1984; 98(4): 209-15
13. Fouriaud C, Salord MCJ, Degoulet P, Aime F, Lang T, Larprughe J, Prades AM, Larprugne J, Prades A, Phalente J. Influence of socioprofessional conditions on blood pressure level and hypertension control. Am J Epidemiology 1984; 120: 72-86.
14. Harrison's Principle of Internal Medicine 10th Edition 589: 1983.

Cancer Society of Kashmir is being established in March 1999.

For details contact:

Prof. Ashiq Hussain

Prof. in CVTS & Surgery Department
Govt. Medical College, Srinagar Kashmir 190 010

INCIDENCE OF CAESAREAN SECTION - A HOSPITAL BASED STUDY

Fazili Farooq M.Ch.; Hakeem Khalida M.Ch.

Abstract : *The present study reveals the incidence of caesarean section in our hospital and various factors influencing it. A high incidence of (20.16%) caesarean section (C.S) have been observed. The C.S rate is high in young mothers (45.15%) and in Primi Gravida's (48.88%) as compared to 2nd and 3rd Gravida. C.S rate is low in preterm (2.80%) and in post term (4.29%) pregnancies as compared to full term pregnancy (92.91%) and in post term (4.29%) pregnancies as compared to full term pregnancy (92.91%). Emergency caesareans have been more (76.50%) as compared to elective caesareans. Acute foetal distress (47.95%) and repeat caesareans (20.53%) are found the most common indications for caesarean section. In previous caesareans the most common indications for C.S found were previous two caesareans (55.46%), pr. LSCS with obstructed labour (12.73%) and pr. LSCS with acute foetal distress (11.82%).*

Key words: *Caesarean section (C.S), Obstructed labour, Acute foetal distress.*

JK-Practitioner 1999; 6(2): 139-141

Introduction

Caesarean section is the most commonly performed surgery in obstetrics. There has been progressive increase in the incidence of caesarean sections during the recent period which may be contributed to various factors like increased safety of the operation due to improved anaesthesia, availability of blood transfusion and antibiotics[1]. Apart from these, the factors like increased awareness of fetal well being, identification of at risk mothers; increasing fear of lawsuits[2] and other factors made caesarean section as a safe alternative to risky vaginal deliveries, thus increasing its incidence. As such due consideration should be given not only to the immediate safety of the mother and her unborn but also to her remote obstetric future.

The present study was undertaken with the objective to finding the incidence of caesarean sections in our hospital and various factors influencing it in our setup.

Material and Methods

The present study was conducted in Community Medicine department (M.C.H Unit) of S.K Institute of Medical Sciences (SKIMS), Srinagar, Kashmir from Ist January, 1996 to 31st December, 1996. All cases delivered by caesarean section during the study period were studied in detail. For each mother the data collected included general particulars like; residence, age and occupation and obstetric particulars like; parity, gestational age, antenatal care and history of any pregnancy related or non related diseases in mother during the antenatal period. Apart from these various indications of caesarean section were also noted separately. The data is tabulated and analysed to give the results.

Observations

During the one year study period, total of 2659 deliveries were conducted in our hospital. Out of these 2123 mothers had normal vaginal delivery and rest 536 mothers delivered by caesarean section, thus giving the incidence rate of caesarean section as 20.16%.

During the study period we had 58 intra-uterine deaths giving the still birth rate of 21.81/1000 total births. There were 22 twin and one triplet delivery out of which 20 twins delivered by normal vaginal delivery and two twins were having Ist transverse twin for which caesarean section was done. 14 mothers delivered their babies by breech.

Table No.1 shows various maternal factors in relation to caesarean section. It is observed that there is high caesarean section rate of 45.15% in young mothers having less than 30 years of age and 48.88% in primi Gravida's as compared to 2nd and 3rd Gravida. There is least caesarean section rate in Gravida 4 and above (8.96%). Further, it is observed that, the caesarean section rate is low in preterm (2.80%) and post term pregnancy (4.29%) as compared to full term pregnancy (92.91%).

There have been more emergency caesareans (76.50%) as compared to elective caesareans during the study period.

From the Department of Community Medicine SKIMS Soura, India (Farooq, Khalida)

Received March 1997 Accepted February 1998

Correspondence to: Dr. Farooq Fazili, Senior Resident (MCH) Department of Community Medicine SKIMS, Soura, Kashmir India, GPO Post Bag No. 27.

Table No.2 shows various indications of caesarean sections. Acute foetal distress is the most common (47.95%) indicatioon for caesarean section. All cases who were having foetal bradycardia, tachycardia, irregular foetal heart, or muconium stained amniotic liquor were taken as acute foetal distress. 20.53% of previous caesareans landed in repeat caesarean section. Failed trial of vaginal delivery was indication for caesarean section in 11.38% of cases. Whereas cephalo pelvic disproportion and breech presentations were indicatio for caesarean section in 5.22% and 4.86% of cases respectively. Other indications for caesareans were APH (2.61%), prolonged leaking with non progress of labour (2.61%), transverse lie (1.50%) and others as is shown in the Table.

Table No.3 shows indication of caesarean section in previous caesareans. Previous 2LSCS was the most common indication for caesarean section in 55.46% of previous caesarean cases. Previous caesarean with obstructed labour was an indication in 12.73% of cases, out of which 4 cases had impending rupture of uterus with thinned down lower segment. Previous caesarean with acute fetal distres was an indication in 11.82% of cases. There were 12 cases (10.90%) of previous caesareans with high risk pregnancy like, toxemia of pregnancy and pregnancy with diabetes and heart disease, where 'as 6(5.45%) cases were as previous caesarean with breech presentation and 4 cases (3.64%) were previous 3 caesareans for which repeat caesarean was done.

Discussion

During the one year study period, high incidence rate of caesarean sections (20.16%) have been observed (Table 1), there are many reasons for this and they have already been mentioned. But still, the rate in our hospital is higher than others. Bhide A. G[2]. (1989-90) have found the caesarean rate of 9.05%, where as K.C. De et al[3] have observed caesarean rate of 15.60% in 1987 at Eden Hospital Calcutta. High incidence of caesarean section in our hospital may be attributed to the fact that our hospital is a referral hospital and at risk cases are dealt here thus increasing the chances of caesareans more.

It is also observed that young mothers (<30 years) had high caesarean rate as compared to older age group. This may be attributed to the fact that this younger group ismore fertile than older age group and further most women complete their family in immediate post marital period as is also evident from the rate of caesareans in relation to Gravidity where high incidence of caesarean was found in Gravida 1, 2 and 3.

Preterm and post term pregnancy had low incidence of caesareans as compared to full term cases. The most common indication in preterm pregnancies for caesarean was APH, where caesarean was done to prevent the maternal mortality. In cases of post term the reason for caesarean was failed trial of vaginal delivery or acute foetal distress.

Very high incidence of emergency caesareans (76.5%) was found in our study. The reason being that there were more cases where either foetus or mother was at risk at the time of delivery, for which emergency caesarean was to be done to save both mother and child, which is also evident from the various indication of caesarean section in Table 3. Our findings are in accordance with Saili A et al (1990)[4] who also have observed high rate of emergency caesareans as compared to elective caesareans (103 out of 121 caesareans).

Table 3 shows that acute foetal distress (AFD) and repeat caesarean sections are the most common indications for caesarean section and the observations are in accordance with Bhide A.G.[2] who also have observed AFD and repeat caesarean as the most frequent indications for caesarean section. Failed trial of vaginal delivery accounted for 11.38% of caesarean sections, while as cephalo pelvic disproportion and breech presentation were indications of caesarean section in 5.22% and 4.86% cases respectively. The lower incidence of such caesareans was also observed by Bhide A.G. (1992)[2] in his study at Nowrosjee Wadia Maternity, Bombay.

The incidence of repeat caesarean in our study was 20.53%. The finding is in agreement with that of Bhide A.G. (1992)[2] who in his study observed the repeat caesarean rate of 19.66% in 1990 and in another study Allahebadia et al (1989)[7] have also observed the repeat caesarean rate of 24.2%. In contrast Arora Rakhsa et al (1992)[5] and Dhal et al (1987)[6] have observed repeat caesarean rate of 59.42% and 50.2% respectively. The reason of high rates in these studies being that trial for vaginal deliveries was not given much to the patients with previous scar. Whereas in our study trial for vaginal delivery was given a good consideration.

Arora Raksha et al (1992)[5] in her study has observed the cephalo pelvic disproportion (CPD) as most frequent indication of repeat caesarean (44.42%) and followed by previous 2 caesareans (6.28%) which is in contrast to our study. The incidence of high risk cases as an indication for repeat caesarean in the study of Arora Raksha et al (1992)[5] has been above 15% which is slightly higher than found in our study (10.90%).

Table-1: Various Maternal Factors in Relation to Caesarean section

Maternal factors	No.	%age
A. Maternal age (year)		
20-25	242	45.15
25-30	156	29.10
30-35	90	16.80
> 35	48	08.95
B. Gravidity		
G1	262	48.88
G2	118	22.01
G3	108	20.15
G4	37	6.90
G5	6	1.12
> G5	5	0.94
C. Gestational age (weeks)		
28-36 (pre-term)	15	2.80
37-40 (full term)	498	92.91
> 40 (post term)	23	.4.29

Table-2: Various indications of caesarean sections

No.	Indication	No.	%age
1.	Acute foetal distress (AFD)	257	47.95
2.	Repeat caesareans	110	20.53
3.	Failed trial of vaginal delivery	61	11.38
4.	Cephalo pelvic disproportion (CPD)	28	5.22
5.	Breech presentations	26	4.86
6.	Antepartum haemorhage (APH)	14	2.61
7.	Prolonged leaking withnonprogress of labour	14	2.61
8.	Transverse lie	08	1.50
9.	Precious baby with bad obstetric history	07	1.30
10.	Cervical dystocia	05	0.93
11.	Brow presentation	04	0.75
12.	Cord prolapse	01	0.18
13.	Rupture uterus	01	0.18
	Total	*536*	*100.00*

Table-3: Indications in repeat caesarean sections

S.	Indication	No.	%age
1.	Pr. 2LSCS	61	55.46
2.	Pr. LSCS with obstructed labour (impending rupture in 4 cases)	14	12.73
3.	Pr. LSCS with acute foetaldistress	13	11.82
4.	Pr. LSCS with high risk pregnancy (PET Diabetes & H.D)	12	10.90
5.	Pr. LSCS with breech presentation	06	05.45
06.	Pr. 3 LSCS	04	03.64
	Total	*110*	*100.00*

LSCS - Lower segment caesarean section.
PET - Pre-eclemptic toxemia.
H.D - Heart disease.

References:

1. D.C. Dutta. Caesarean section Text Book of Obsttrics Chap 36. Pub. New Central Book Agency, Calcutta- 700009 India-1993.
2. Bhide A.G. Caesarean section: How safe is it? Journal of Obstetrics and Gynaecology 1994(3): 330-33.
3. K.C.De, J. Mukherjee, Biman C. Roy, Provas Das. Study of Breech - outcome in relation to parity and mode of delivery. Journal of Obstetric and Gynaecology 1992; 42(2): 460-64.
4. Saili A, M.S. Sama, D. Haldar, S. Kumari, A.K. Dutta. Delayed caesarean section: Neonatal outcome. India Pediatrics June, 1990; 27: 601-604.
5. Arora Rakhsa, Asha P. Rajaram. Oumachiguijosephine-outcome of post caesarean pregnancy in a tertiary Insitutue in South India. Journal of Obstetric and Gynaecology 1992; 42(3): 334-339.
6. Allahabadia G.N., Ambiye V.R. Shambaug A: M.J Obstet Gynaecol India 1989; 39: 782.
7. Dhall K. Mittal S.C. Grova V. and Dhall G.I. Internat J Gynaecol Obstet 1987; 25: 199.

HOLT-ORAM SYNDROME - REPORT OF A FAMILY

Abdul Hamid Zargar M.D., D.M.; Arshad Iqbal Wani M.D.; Mir Iftikhar Bashir M.D.; Mohammad Ashraf Ganai M.D.
Bashir Ahmad Laway M.D.; Shariq Rashid Masoodi M.D.

Abstract : *Congenital heart disease complicates approximately 1 percent of all births. These usually are the result of aberrant embryonic development of a normal structure, or failure of such a structure to progress beyond an early stage of embryonic or fetal development. Malformations are due to complex multifactorial genetic and environmental causes. If properly looked for, cardiac involvement may be one component of a multiple system involvement. There are some congenital heart diseases which are associated with musculoskeletal abnormalities. One such disorder is Holt-Oram syndrome, an autosomal dominant disorder characterised by upper limb dysplasia, atrial septal defect and marked variability within families. In this report we describe one such family.*

Key Words: Autosomal dominant; Holt-Oram Syndrome; Limb dysplasia; Congenital heart disease.

JK-Practitioner 1999; 6(2): 142-144

Subjects and Methods:

A couple (RB, 41 years female, and IK, 43 year old male) were married in 1976 and produced seven children (A-G) (Fig 1). They brought three of these children to the endocrine clinic with complaints of multiple skeletal abnormalities and failure to thrive. The mother (RB) was a diagnosed case of primary hypothyroidism on thyroxine replacement and a private practitioner had advised an endocrine evaluation of her children with skeletal deformities.

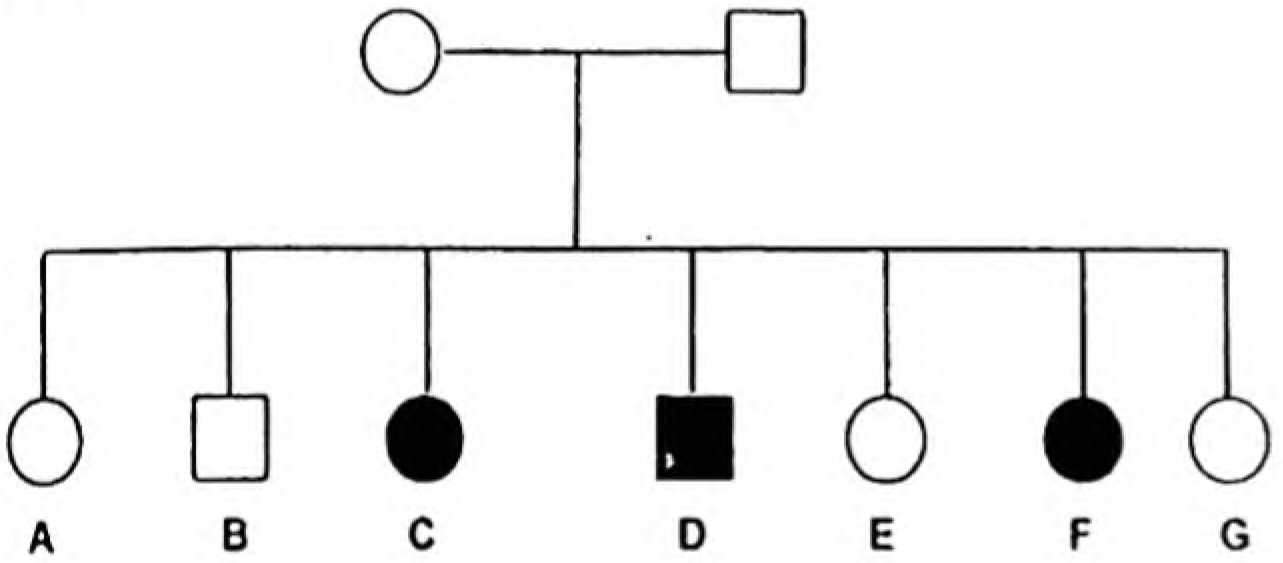


Fig. 1. Family Pedigree

The siblings A,B,E and G were apparently normal and routine clinical examination did not reveal any abnormality.

Subject C, a 10 year old female, 3rd in birth order was a product of normal conception and home delivery. Mother had consumed some abortifecient (herbal medicine) during third month unsuccessfully. Otherwise she had consumed no medicines and had not consulted a doctor during her pregnancy. At the time of delivery parents noticed shortening of the upper limbs with some deformities. The child otherwise grew normally. Clinical examination revealed an adolescent female with a height of 135 cms (upper segment 67 cms and lower segment 68 cms), high arched palate, pulse 74 BPM and blood pressure 100/70mmHg. Her upper limbs, particularly forearms, were short. She had only four fingers with one webbed digit on both sides. Her lower limbs were normal. Apart from mild conjunctival pallor, rest of the systemic examination was normal.

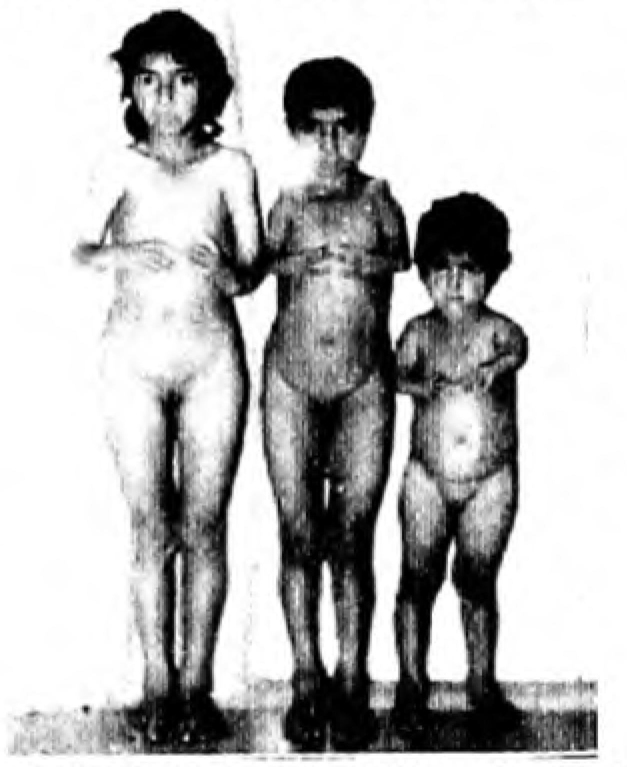


Fig.2 Photograph of the affected subjects (C.D and F). C-Left: D-Center: F-Right.

Subject D, an 8½ year old boy, 4th in birth order was a product of uneventful home delivery. Parents noticed some musculoskeletal abnormalities in the child at birth. He grew normally except that he had frequent respiratory tract infections and dislocated his shoulder once which needed medical attention. Clinical examination revealed high arched palate, grade II thyromegaly, clubbing of fingers and a height of 126 cms (upper segment 64 cms, lower segment 62 cms). He had drooping shoulders, dislocated shoulder on left side, malformed clavicles and absent forearm on the right side[4] with malformed hands having only three digits on either side. Cardiovascular examination revealed a precordial bulge with left parasternal heave, a grade III

From the Department of Endocrinology and Internal Medicine, SKIMS Soura, Srinagar, Kashmir. (Zargar, Wani, Bashir, Ganai, Laway, Masoodi)

Received December 1998 Accepted March 1999

Correspondence: Professor Abdul Hamid Zargar. Head of Deptt. of Endocrinology SKIMS P.O.Box: 1098, GPO, Srinagar-1 Kashmir (India)

systolic murmur best heard in the pulmonary area and a fixed split second heart sound.

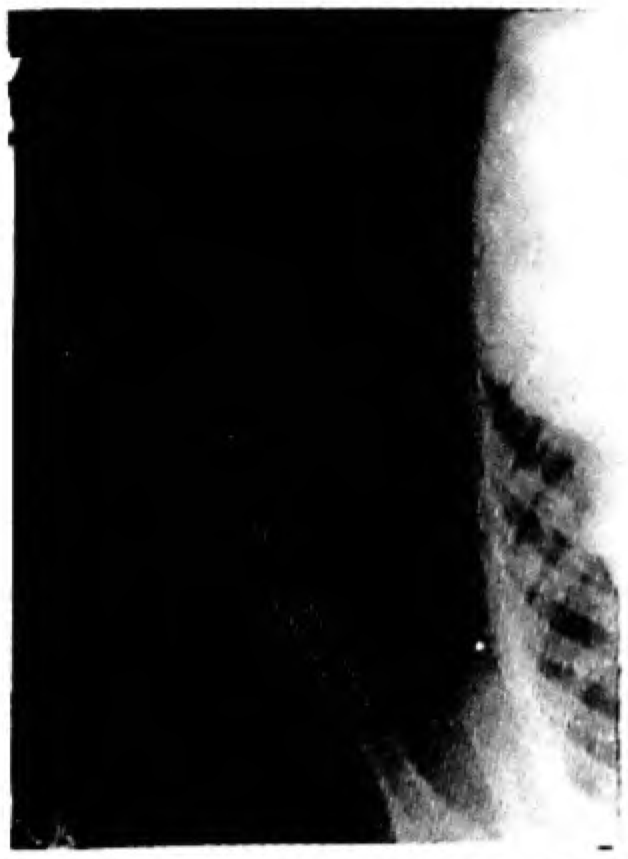
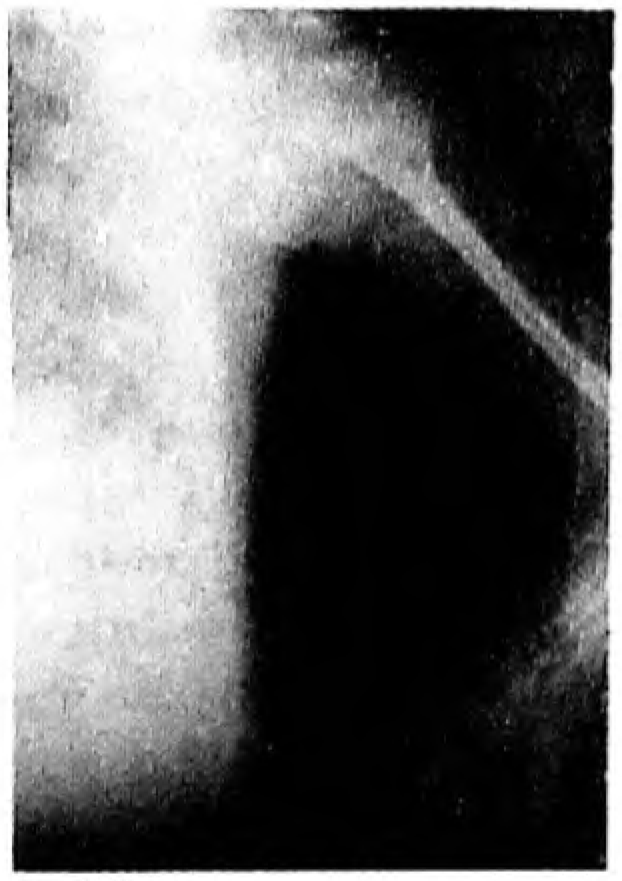


Fig.3a. X-ray arm of subject C.

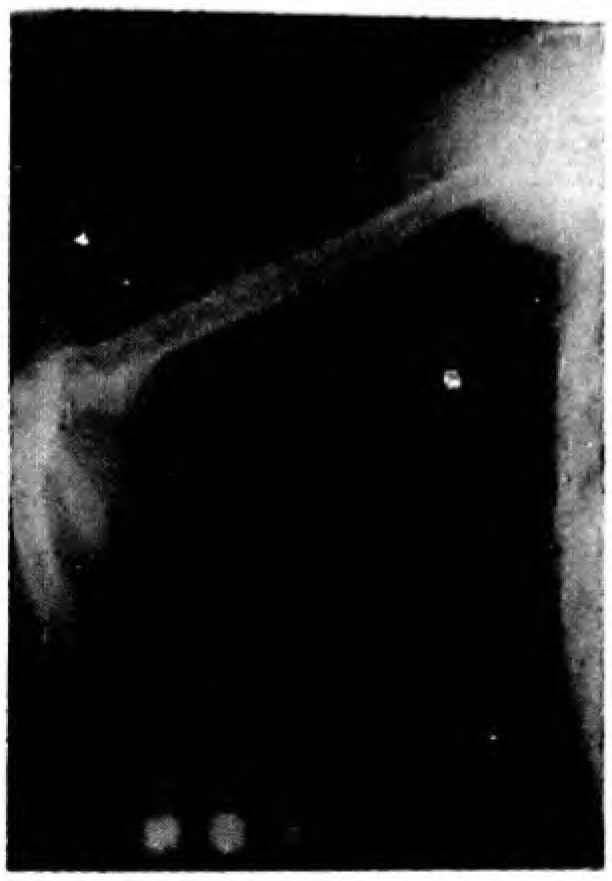
Subject F, a 4½ year old female child, 6th in birth order was also noticed to have skeletal abnormalities at birth. Her clinical examination revealed high arched palate, a height of 108 cms (upper segments 57 cms, lower segment 51 cms), grossly short upper limbs with deformities of both hands characterised by four digits on either side with webbing of two fingers on left side. Systemic examination revealed a short systolic murmur in pulmonary area with wide and fixed splitting of second heart sound.

A detailed family history revealed that the maternal grandfather of these children had some skeletal abnormalities, had fathered seven children five of whom had died at a young age.



3b. X-ray arm of subject D.

Investigations performed on these subjects included a detailed hemogram, urine examination, routine serum chemistry including blood glucose, blood urea, nitrogen, serum creatinine, calcium, phosphorus, alkaline phosphatase, SGOT, SGPT and serum electrolytes. Detailed radiological screening including X-ray chest P/A view, X-ray hands, arms and shoulders was performed. A 12 lead electrocardiogram and 2D echocardiography was performed in all the three subjects. Serum tri-iodothyronine (T_3), tetraiodothyronine (T_4) and thyroid stimulating hormone (TSH) were estimated in all the three subjects in view of thyromegaly in one subject and maternal history of hypothyroidism.



3c. X-ray arm of subject E.

Table 1: Clinical characteristics of the siblings

Subject	Sex	Age (in year)	Height (in cms)	Expected height (im cms)
A	F	19	157	159
B	M	17	168	170
C	F	10	1135	136
D	M	8½	126	127
E	F	6	112	114
F	F	4½	108	104
G	F	2	88	87

Results

Table 1 gives the clinical characteristics of this family. Linear growth of the individuals with musculoskeletal abnormalities in the upper limbs was not compromised. Apart from hypochromic microcytic anemia in subject C, no other abnormality could be detected in their hemogram and serum chemistry. Serum T_3, T_4, and TSH levels were normal in all subjects.

Radiological evaluation in the affected subjects (C,D and F) revealed:

Subject C: Short forearm bones with 4 metacarpals. (Fig. 3a)
Subject D: Short forearm bones with only 3 metacarpals. (Fig. 3b)
Subject F: Short forearm bones with 4 metacarpals. (Fig. 3c).

Electrocardiogram revealed juvenile pattern in all the three affected subjects. Echocardiography revealed atrial septal defect in subjects D & F.

Discussion

Holt-Oram syndrome was first described in 1960[1]. The cardinal manifestations of this disorder include autosomal dominant transmission, upper limb dysplasia, atrial septal defect and marked variability within families[2]. In heterozygotes for the mutation, arm deformity ranges from undetectable through distally placed thumbs and hypoplastic thenar eminences, triphalangeal thumbs, anomalies of the carpus and radial aplasia, to phocomelia and hypoplasia of the clavicles[3].

The family described in this report had classical presentation of an autosomal dominant disorder. Three of the seven siblings were affected. There was history of some skeletal abnormalities in the maternal grandfather. However, the mother did not have any overt skeletal and cardiovascular manifestations of this syndrome. As she did not cooperate for detailed radiological survey, less overt bony abnormalities in her could not be excluded. Affected siblings had a heterogenous spectrum of musculo-skeletal abnormalities. In this disorder, the upper extremity deformity is usually bilateral but may be asymmetrical in severity, with the left side affected more[4].

The atrial involvement ranges from none to a large secundum defect with early severe hemodynamic compromise[4]. Other cardiac malformations have been reported, with ventricular septal defects the most frequent. Two forms of atrial septal defects exist. One form has no other associated abnormalities and is speculated to be a chromosmal 6p linked to the HLA complex; it is as yet unconfirmed by genetic linkage analysis[5]. Another form is the one associated with skeletal abnormalities known as Holt-Oram syndrome. One gene for Holt-Oram syndrome has been mapped to 12q2[5-7]. The responsible gene has been identified[8,9]. Another form of familial atrial septal defect has also been described, thought to be due to mitochondrial inheritance[10].

The diagnosis of Holt-Oram syndrome is most likely to be missed in a patient with an unknown or unremarkable family history, secundum septal defect, and minimal or no thumb anomaly. In any case of an atrial septal defect, the patient and the parents should be carefully examined for limb malformations and the family history studied in detail.

References:

1. Gall JC, Stern AM, Cohen MM et al. Holt-Oram syndrome: clinical and genetic study of a large family. Am J Hum Genet 1966; 18: 187.
2. Smith AT, Sack GH. Taylor GJ. Holt-Oram syndrome. J Pediatr 1979; 95: 539-534.
3. Towbin JA, Roberts R. Cardiovascular diseases due to genetic abnormalities. In; Alexandar RW, et al (eds.) Hurst's: The Heart, 9th Edition, McGraw Hill, New York, 1998;1877-1923.
4. Pyeritz RE., Genetics and cardiovascular disease. In: Braunwald E, (ed). Heart Disease: A Textbook of Cardiovascular Medicine 5th Ed. W.B. Saunders 1997; 1650-1686.
5. Basson CT, Cowley GS. Solomon SD, et al. The clinical and genetic spectrum of Holt-Oram sydrome (heart hand syndrome). N Engl J Med 1994; 330: 885.
6. Bonnet D, Pelet A, LOegeai-Mallet L, et al: A gene for Holt-Oram syndrome maps to the distal long arm of chromosome 12. Nature Genet 1994;6:405.
7. Terret JA, Newbury-Ecob R, Cross GS. et al. Holt-Oram syndrome is a genetically heterogenous disease with one locus mapping to human chromosome 12q. Nature Genet 1994; 6:401.
8. Basson CT, Bachinski DR, Lin RC, Levi T, Elkins JA, Soults J, et al. mutations in humans cause limb and cardiac malformations in Holt-Oram syndrome. Nature Genet 1997; 15:30-35.
9. Li Qy, Newbury-Ecog RA, Terret JA. Wilson DI, Curtis ARJ, Yi CH, et al: Holt-Oram syndrome is caused by mutations in TBS 5, a member of the brachyury (T) gene family. Nature Genet 1997;15:21-29.
10. Sherman J, Angulo M, Boxer RA, Glucck R. Possible mitochondrial inheritance of congenital cardiac septal defects. N Engl J Med 1985: 313: 186-187.

DECLARATION UNDER SECTION 5 OF THE PRESS AND REGISTRATION BOOKS ACT OF 1967 AS AMENDED FROM - I (SEE RULE I)

1. Title - JK-PRACTITIONER
2. Place of publicaton - Srinagar
3. Periodicity of publication - Quarterly
4. Publisher's name - Dr. G.M. Malik
Whether Citizen of India - Yes
Address : Jhelum Market, Batmaloo, Srinagar - 190 010, Kashmir (India)
6. Editor's Name - Dr. G.M.Malik
Citizen of India - Yes
Address : Jhelum Market, Batmaloo, Srinagar - 190 010, Kashmir (India)
7. Particulars of other individuals who are owners/share holders of Newspaper.

I Dr. G.M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

Sd/-

Dr. G.M. Malik

HYDATED CYST OF BRAIN- A CASE REPORT AND REVIEW OF LITERATURE

M.A. Wani, M.S., M.Ch.; M.L. Babu, M.S; A.G. Ahanger, M.S., M.Ch.; A.R. Kirmani, M.S.; R.K. Saxena, M.S., M.Ch.;

Abstract: *Primary hydatid cyst of the brain is a rare cause of Intracranial Space Occupying Lesion. The case history and clinical features of a 10 years old boy are presented. This child presented with clinical features suggestive of raised intracranial tension. Cerebral angiography was performed (CT scan facility was not available in 1966) which revealed a parietal avascular cystic lesion. Diagnosis of hydatid cyst was made at Surgery. The patient did not have any evidence of hydatid disease anywhere else in the body.*

Key Words: *Brain cyst; Hydatid cyst- Echinococcosis; Parasitic cyst; Angiogram; Raised Intracranial Tension.*

JK-Practitioner 1999; 6(2): 145-146

Introduction

In our region where Hydatid disease is not so prevalent, primary hydatid cysts of the Brain are rare.[1] These cysts present with clinical features of cerebral compression. In countries where Hydatid disease is prevalent, cerebral hydatid cysts may be responsible for as much as 10%[2] of all intracranial space occupying lesion[2,3,4]. In countries where hydatidosis is not so prevelant it accounts for about 2% of all intracranial space occupying lesions[5,6,7,8]. These cysts are rare in adults and accounts for approximately 5% of all echinococcosis cases showing evidence of infestation during child hood. These cerebral cysts are usually single, spherical, unilocular and may be large[10].

Case Report

A 10 year old boy from a rural community presented with symptoms suggestive of raised intracranial pressure, which had persisted for six months. The parents reported that the child demonstrated a slight limp during walking. At the time of examination the boy was febrile. The general physical and systemic examination was unremarakable. Neurologically, he was concious and oriented. He had a left-sided spastic hemiparesis with grade 4 (MRC scale) motor function with up-going planter. The fundus demonstrated papilledema. Laboratory examinations were essentially normal. X-rays of the chest and skull were reported to be normal. Echoencephalography (A-mode scan) showed a midline shift to the left. An isotopic brain scan with hemispheric blood flow measurements was unremarkable. A cerebral angiogram suggested a large right Parietal cystic avascular mass (Fig. I).

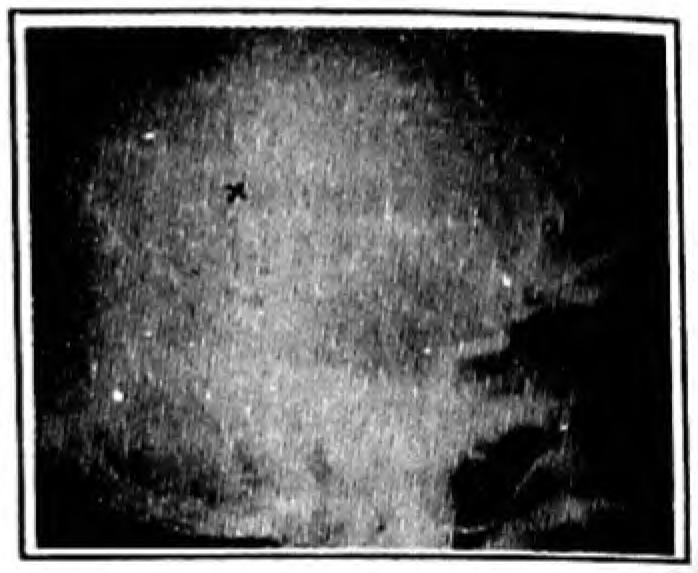


Fig.I: Cerebral angiogram suggestive of an avascular lesion in the parietal area

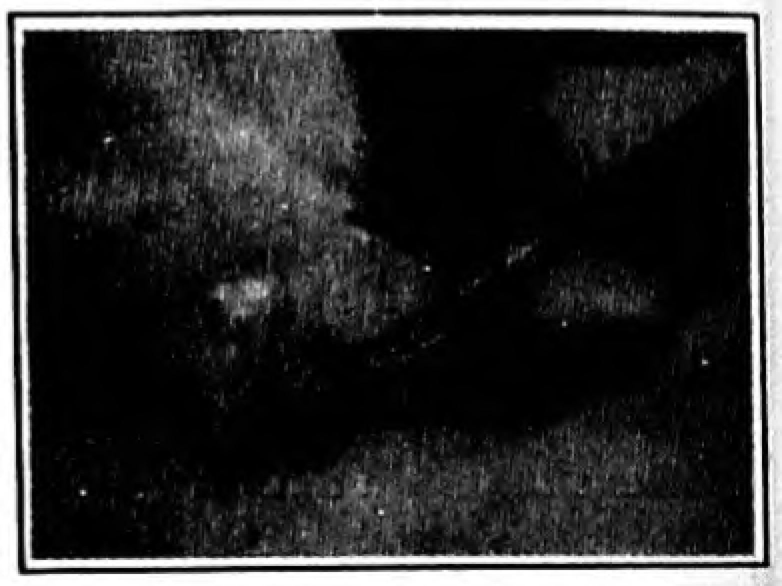


Fig.II: Cortical incision has been made and the intact cyst is partly visible

Repeated ESR showed a slight rise, although total and differential leukocyte counts were normal. He was operated upon under antibiotic cover. Osteoplastic craniotomy revealed a thin calvarium. The dura was tense, hence osmotherapy was given to decrease intracranial tension. When the dural flap was turned, a subcortical lesion became visible through the overstretched cortex. A small cortical incision revealed a glistening, pearly white cystic lesion, which was clearly indicative of the diagnosis of a hydatid cyst. Taking recommended precautions and using the method of Iniquez combined with Dowling's technique, the cyst was delivered slowly from within the brain (Fig.2). It measured 9x7cm. The histological findings confirmed our intraoperative impression. The boy's postoperative recovery was uneventful. His hemiparesis improved. Extensive clinical, radiologic, serologic, ultrasound examinations failed to detect any evidence of systemic hydatidosis. The patient remained well after

From the Department of Neurosurgery, Srinagar, India (Prof. Wani, Kirmani, Babu) **and Cardiovascular and Tharacic Surgery** (Ahanger, Saxena) **SKIMS, Soura, Srinagar, India**

Received October 1998 Accepted February 1999

Correspondence to : Prof. M.A.Wani, Head Department of Neurosurgery SKIMS Srinagar, Kashmir P.O.Box 27.

12 years of follow-up.

Discussion

Hydatidosis is a disease that occurs all over the world and is prevalent in cattle and sheep breeding countries with a large number of dogs. There are numerous reports in the literature on the causative parasite, its life cycle, the mode of infection in humans and the natural history of the disease[3,4]. In endemic areas, almost 10% of infected patients may have cerebral cysts[11]. The younger population is most susceptible to this infection. Although the majority of hydatid cysts are located in the cerebral hemispheres, occasional cysts are reported to have been delivered from within the Aqueduct of Sylvius and the sella turcica[12,13]. Most cerebral cysts are usually large and solitary, but cases of multiple cysts are well documented[1,4,14,15]. Alveolar hydatid involvement of the brain (Echinococcus multilocularis) is a well described entity[3,16]. Headache is the usual complaint. The patients may remain asymptomtic for a long time. Symptoms and sings of raised intracranial pressure may develop late. Cysts located in and around the central sulcus region may be associated with seizures[8] or early neurological deficits.

The clinical diagnosis, in endemic areas, is probably not very difficult, but is is more often presumptive in less prevalent areas. The diagnosis on the basis of plain skull X-rays and angiography remains unreliable[8]. The availability of computerized tomography has improved the preoperative diagnosis of cerebral hydatid diasease. Characteristic CT-features suggestive of hydatid brain cysts have been well described[5,17]. An intraparenchymal cystic lesion with smooth walls and clearly defined borders, containing fluid with a Hounsfield value similar to that of CSF, is characteristic of cerebral hydatid cysts[5]. No ring enhancement is observed after contrast injection[17]. Serologic tests may be useful in them are positive, but many patients with cerebral hydatid cysts do not develop an immune response[18]. In cases with primary cerebral cysts, immunologic tests are usually negative and the eosinophil count may also be normal[19]. Treatment of hydatid cysts remains total surgical excision with particular attention to the prevention of rupture[20,21]. The prongosis after excision of a primary solitary hydatid cyst of the bain is excellent. It is less favourable in patients with multiple cysts because it may be difficult to remove deeper and smaller cysts without rupture[8]. Although surgical excision of alveolar hydatid cysts of the brain is rewarding, prognosis remains poor in the presence of systemic evidence of the disease[16].

References:

1. Sherma S.C; Ray R.C. Primary Hydatid cysts of the Brain in an Adult: Report of a case. Neurosurgery, 1988; 3: 374-376.
2. Hamit Z. Gokalp and Ahamet Erdogan. Hydatid cyst of the aqueduct of sylvius. Case Report. Clin. Neurol. Neurosurg. (1988); Vol. 90-1:83-85.
3. Arana-Iniquez R: Echinococcus, in: Vinken PJ, Bruyn GW (eds.): Infections of the Nervous System, Part III. Handbook of Clinical Neurology, Vol. 35. Amsterdam, New York. Oxford: North-Holland, 1978, pp 175-208.
4. Carrea R, Dowling E Jr, Guevara JA: Surgical treatment of hydatid cysts of the central nervous system in pediatric age (Dowling's technique). Child's Brain 1975; 1: 4-21.
5. Abbassion K, Rahmat H, Ameli NO, Tafezoli M: Computerized tomography in hydatid cyst of the brain. J Neurosurg 1978; 49: 408-411.
6. Balasubramanium V, Ramanujam PB, Ramamurthi B: Hydatid disease of the nervous system. Neurol India 18: (Suppl. 1): 1970: 92-95.
7. Dharkar SR, Dharker RS, Vaishya MS, Sharma ML, Chourasia BD: Cerebral hydatid cysts in central India. Surg Neurol 1977; 8: 31-34.
8. Sharma A, Abraham J: Multiple gaint hydatid cysts of the brain. J Neurosurg 1982; 57: 413-415
9. Dew HR: Primary cerebral hydatid disease. Aust NZ J Surgery 1955; 24: 161-171.
10. Ramsay PG; Plorde JJ: Cestode infection in Braunwald E. (Eds.) Harris OW, Principles of Internal Medicine, New York, McGrew Hill 1987- Ed. 11, 825-829.
11. Hamza R, Tohibe S, Jamoussi M, Bardi-Bellagha I, Chitioui R: Intracranial and orbital hydatid cyst. Neuroradiol 1982; 22: 211-214.
12. Gokalp HZ, Erdogan A: Hydatid cyst of the aqueduct of Sylvius. ClinNeurol Neursurg 1988; 90: 83-84.
13. Ozgan T, Bertan V, Kansu T, Sema A: Intrasellar hydatid cyst. Case report. J Neurosurg 1984; 60: 647-648.
14. Kaya U, Ozden B, Turker K: Intracranial hydatid cysts. Study of 17 cases. J Neurosug 1975; 42: 580-582.
15. Slim MS, Khayat G, Nasr AT, Jidejian YD: Hydatid disease in childhood. J Pediatric Surg 1971; 6: 440-448.
16. Aydin Y, Barlas O, Yolas C, Aydin IH, Ceviz A, Aldag A, Ohen D, Akdemir D: Alveolar hydatid disease of the brain. J Neurosurg 1986; 65: 115-119.
17. Oagan T, Bertan V, Kansu T, Sema A: Intrasellar hydatid cyst. Case report. J Neurosurg 1984; 60: 647-648.
18. Sharma S, Ray RC: Primary hydatid cyst of the brain in an adult: Report of a case. Neurosurg 1988; 23 (3): 374-376.
19. Pinon JM: Immunological study of hydatidosis: Amer J Trop Med Hyg 1979; 28: 318-319.
20. Arana-Iniquez R, Lopz-Fernadez JR: Parasitosis of the nervous system with special reference to echinococcosis. Clin Neurosurg 1967; 14: 123-144.
21. Saidi P, Nazarian I: Surgical treatment ofhydatid cyst. N Engl J Med 1971; 274: 1346-1348.

SPORADIC OCCULOPHARYNGEAL MUSCULAR DYSTROPHY WITH OPTIC ATROPHY

S.M.Saleem D.M.; Abdul Majid Wani M.D.; Sonaullah Shah M.D.; Azra Shah M.D.

Abstract: *Occulopharyngeal muscular dystrophy constitutes a subgroup of progressive external opthalmoplegia (PEO), optic atrophy is a very rare association of PEO[3]. We report a 65 year old man as a rare sporadic case of occulopharyngeal muscular dystrophy with optic atrophy.*

Key words: *Progressive external ophthalmoplegia, Muscular dystrophy, Optic atrophy*

JK-Practitioner 1999; 6(2): 147-148

Introduction

Progressive external opthalmoplegia should meet the five criteria[1]:

> *Progressive external ophthalmoplegia prominent dysphagia family with docmented autosomal inheritance typical nuclear inclusions and no RRF (red-ragged fibres) beyond the number encountered in asymptomatic people.*

About two thirds of all progressive external ohpthalmoplegia (PEO) patients show facial weaknes and many also note dysphagia. Dysphagia and dysarthria are often mild but may be severe as in French Canadian form, first described by Taylor (1915). This latter form has an autosomal dominant inheritance and seems to have resulted from multiple DNA mutations. Histological changes include Z-line streaming and disorganization of sarcomere; replacement by fat and fibrous tissue; nuclear tubulofilaments 8.5 nm in diameter (Tome bodies); rimmed vacuoles and non-specific mitochondrial changes[2]. Optic atrophy is a very rare association of PEO[3]. Meire et al (1985) described a syndrome of PEO, optic atrophy and hearing loss[4].

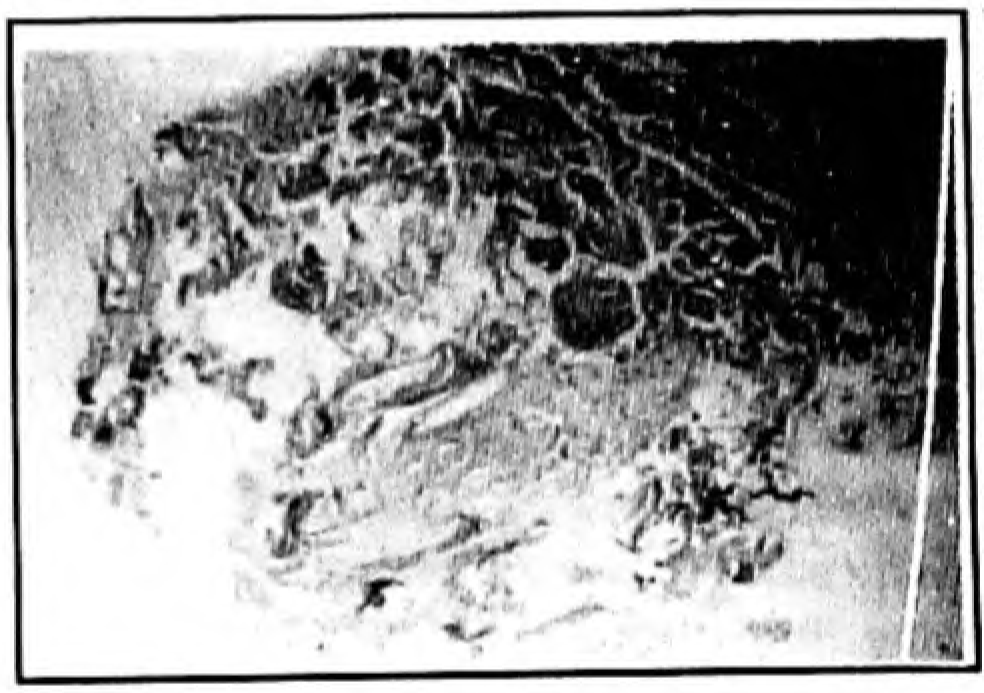
We present a case report of occulopharyngeal muscular dystrophy with optic atrophy with no family history of such disease.

Case Report

65 year old man, tobacco smoker detected hypertensive 3 years back and on erratic treatment, non-diabetic and no occupational exposure or drug intake presented with the complaints of:

1. progressive drooping of eyelids - 7 years
2. inability to look in all the planes - 7 years
3. progressive diminution of vision - 5 years.

In addition, patient had developed difficulty in swallowing solids, dribbling of saliva and dysarthria. Patient denied any history of weakness of any other part of body, bladder or bowel in-continence, emotional liability and any excacerbration or remission of above symptoms. Examination revealed pulse of 84/mt. regular, B.P. of 150/98 mmHg, respiratory rate of 18/mt. Chest, CVS and abdominal examinations were normal. Patient had bilateral ptosis, weakness of eye movements in all the planes, visual acquity of 6/36 (R) and 6/60 (L), eye. Pupillary reflexes and gag reflex were normal. Patient had dysarthria and rest of the neurological examination was normal. Fundus examination revealed bilateral disc pallor. Patient's haemogram, serum biochemistry including muscle enzymes were normal. CXR, ECG, CAT scan head were normal. T3, T4, TSH and serum and CSF immunoglobulines were normal. Collagen vascular profile and VDRL were negatie. EMG was a normal study. Neostigmine test was negative. Muscle biopsy revealed (Fig 1):



1. Degneration of muscle fibres with replacement by fibrous tissue and fat (H&E x100)
2. Degeneration of muscle fibres with frequent hyaline fibres (H&E x100).

From the Department of General Medicine, SK Institute of Medical Sciences, Srinagar - 11, India (Saleem, Wani, Shah) **Deptt. of Pathology** (Azra) **SKIMS.**

Received December 1997 Accepted December 1998

Correspondence to : Dr. S.M.Saleem, Muhajid Manzil Srinagar - 190 002, Kashmir

Discussion

Muscular dystrophy refers to a group of hereditary progressive diseases. Each type of muscular dystrophy has unique phenotypic and genotypic features[3] Occulopharyngeal muscular dystrophy (OPMD) represents one of the distinct disorders presenting with progressive external opthalmoplegia (PEO). It has an autosomal dominant inheritance with complete penetrance. Patients usually present with ptosis and/or dysphagia in 5the to 6th decade[3]. About two-thirds of all PEO patients show facial weakness and many also note dysphagia.

French-Canadian form of OPMD is a unique disorder first described by Taylor in 1915 and characterized by later onset, severe dysphagia, dysarthria and autosomal dominant inheritance. 'Tome bodies' the morphological marker of OPMD are (tubulofilamentous inclusions 8.5 nm outer and 3 nm inner diameter) in muscle fibre nuclei first described by Tome and Faradeau in 1980[2].

PEO can occur alone or in combinantion with central multisystem diseases like Kearns-Sayre syndrome, dysphagia and motor neuron disease, peripheral and cranial neuropathy, a-betalipo-proteinemia, celiac disease and defness.

Augustin et al (1984) described optic atrophy as the only neural complication of PEO with out retinopahty[5].

Maire et al (1985) described a similar syndrome of PEO, optic atrophy and hearing loss[4].

The authors find an opportunity to present a unique and rare case with features of OPMD and bilateral optic atrophy, without any pigmentary retinopathy. There is no family history of such illness nor has patient any other neurological involvement like limb or neck weakness.

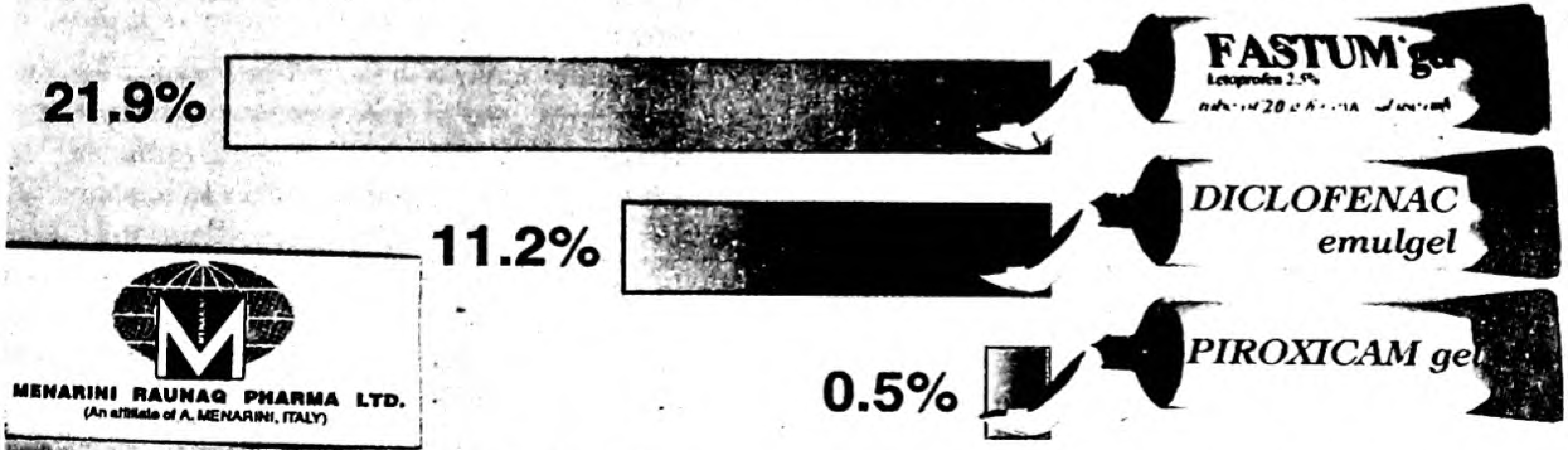
References:

1. Rowland LP and Di Mauro S (editors): Handbook of clinical Neurology, Vol 18 (62); 1992: Myopathies; progressive external opthalmoplegia and occular myopathies pp 287-315.
2. Tome F.M.S. and M Fardeau; Nuclear inclusions in occulopharyngeal muscular dystrophy. Acta Neuropathol 49; (1980): 85-87.
3. Jerry R, Mendell / R. Griggs C. Inherited, metabolic, endocrine and toxic myopathies; Harrison's principles of Internal Medicine 13th ed; vol 2: pp 2383-2386.
4. Meire F, J.J.Delaey, S. De Bie, M. Vanstacy and M.T. Matton: Dominant optic atrophy with progressive hearing loss and chronic PEO. Opthalm Paediatr Genet 5 91985); 91-97.
5. Augstin P, Diyardin M., Daluzean N. and Denis P: (Opthalmoplegia plus with otpic atrophy apropos of a case). Rev. Otoneuro-opthalmoe 56; (1984): 183-189.

"*Due to its optimal penetration,* **FASTUMgel** *has shown strong efficacy in a wide range of conditions such as:*

✓ Backache
✓ Sport Traumatology
✓ Arthropathy

Tissue penetration % of active substance liberated at the end of diffusion through membrane



FASTUMgel
Ketoprofen 2.5% w/w

The innovative hydroalcoholic gel for rapid pain relief

EDWARD'S SYNDROME BABY WITH PORENCEPHALY BORN TO A TOXOPLASMOSIS POSITIVE MOTHER

Mushtaq Ahmad MD; Wajid Ali MD; Masood-ul-Hassan MD.

***Abstract:** A Microcephalic baby was admitted to Neonatal Intensive Care Unit for investigations and management. Mother was Toxoplasmosis positive and cranial USG of the baby showed porencephaly. Baby showed most of the features of Edward's syndrome.*

***Key words:** Edward's Syndrome; Porencephaly; Toxoplasmosis*

JK-Practitioner 1999; 6(2): 149

Case Report:

Microcephalic male baby born after normal delivery was admitted for investigations and further management. Baby was born to a 2nd gravida mother, who is married to her cousin (Consanguinous marriage).

First baby had hydrocephalus and was delivered after destructive operation. Mother was screened for TORCH infection and was found positive for Toxoplasmosis Mother received cyclic treatment of Spiramycin for toxoplasmosis during pregnancy.

On examination:

G.C.	Fair	Head circumference	:	29.4cms
Weight	2.5kg	Crown heel lenghth	:	42.5cms

Upper segment : 22.7 cms, lower segment: 19.8cms
Chest circumference : 19.2cms, Mid arm circm: 8.3cms

Baby in flexion posture. Neonatal reflexes fair. Skull-flat, anterior and posterior fontenelle not felt. Head microcephalic with sloping forehead and lowset bat ears, overlapping of fingers and rocker-bottom feet.

Chest, CVS, Abd. Clinically NAD Fundi (N)

Genitalia - microphallus

Baby had mild jaundice on day 4 of birth which resolved with phototherapy.

Investigations: PCV - 55%, S.Bilirubin-10mg%, Electrolytes and HMG-WNL, SxR & CxR - WNL Torch: Negative, cranial USG showed porencephalic brain.

Baby received incubator care and bottle feeds and was referred to AIIMS, Delhi for MRI and genetic counselling.

Discussion

Edward's syndrome (Trisomy 18) is common next to Down's svndrome with an incidence of 1/8,000 births[2]. Baby presents with low birth weight, microcephaly, micrognathia, low set malformed ears, overlapping of fingers, rocker bottom feet, congenital cardiac and renal defects, mental retardation, increased gyri and heterotopias of neurons. 95% cases are lethal in the first year of life[1,2].

Toxoplasmosis is a common cause of recurrent abortions and the affected liveborn babies present with purpura, hepathosplenomegaly, jaundice, convulsions, hydrocephalus, choreoretinitis and cerebral calcifications[2,3].

Porencephaly refers to the presence of cysts or cavities within the brain that result from developmental defects or acquired lesions including infarction of brain. It represents developmental abnormalities of cell migration and is often associated with other malformations of brain including microcephaly, abnormal pattern of adjacent gyri and encephalocele[12].

In our patient the abnormal features do not fit in Toxoplasmosis but are typical of Edward's syndrome with associated porencephaly. Does any relationship exist between Toxoplasmosis and trisomy 18 is to be ascertained.

References:

1. Barth PG: Disorders of Neuronal Migration. Can. J of Neural Sci. 1987; 14.
2. Behrman, Kleigman, Irvin -Nelson text book of Pediatrics - 15th Edition: 1982; 314: 1618.
3. Stevenson RE, Hall JG, Goodman R.M. Human malformations and related anomalies, Exford, Oxford Monographs on Medical Genetics, 1983.

From the Department of Neonatology, SKIMS, Soura, Kashmir India (Mushtaq, Ali, Hassan)

Received January 1997 Accepted March 1999

Correspondence to: Dr. Mushtaq Ahmad, MD, Deptt. of Neonatology, SKIMS, Srinagar, Kashmir.

JK-PRACTITIONER

ASYMPTOMATIC LONG STANDING IATROGENIC ABDOMINAL FOREIGN BODY - A RARITY

Parveen Malik M.D.; Bilquees Jameela M.D.; Farhat Hameed M.D.

***Abstract:** Iatrogenic abdominal foreign bodies are seen less frequently in day to day practice. We report an asymptomatic long standing case of Iatrogenic abdominal foreing body (IUCD and Curette) which is very rare.*

***Key words:** Foreign body, Intrauterine contraceptive device. (IUCD), Currette.*

JK-Practitioner 1999; 6(2): 150

Case Report

A 45 year old multiparous female consulted an orthopedician for low back ache and radicular pain right lower limb of 1 months duration. Clinical examination was inconclusive except for an absent right ankle jerk. With impression of L5S1 radiculopathy, an X-ray lumbosacral spine AP, lateral view was sought, which revealed anterior wedge collapse of L4-L5 vertebra with normal intervertebral disc space and two abdominal foreign bodies (Fig 1). Few days after this investigation, patient reported to us with lower abdominal pain. On gruelling history she revealed that an intrauterine contraceptive device (IUCD) was kept five years back, which was removed after a period of three years and during that time her menstrual periods were regular. She became pregnant after removal of IUCD, which was terminated at 3 months gestation. Insertion, removal of IUCD and dilatation and currettage were done by a single gynaecologist and patient was symptom free after all these procedurers. In view of her X-ray findings laparotomy was performed under general anesthesia. A broken piece of IUCD and full length currette, one end of which was embedded in the greater omentum, (Fig. II) were recovered from the abdominal cavity. Uterus showed scaring of fundus from where perforation had occured. There were no adhesions and all other viscera were normal. Patient was ligated and abdomen was closed after achieving complete hemostasis. Post operative period was uneventful.

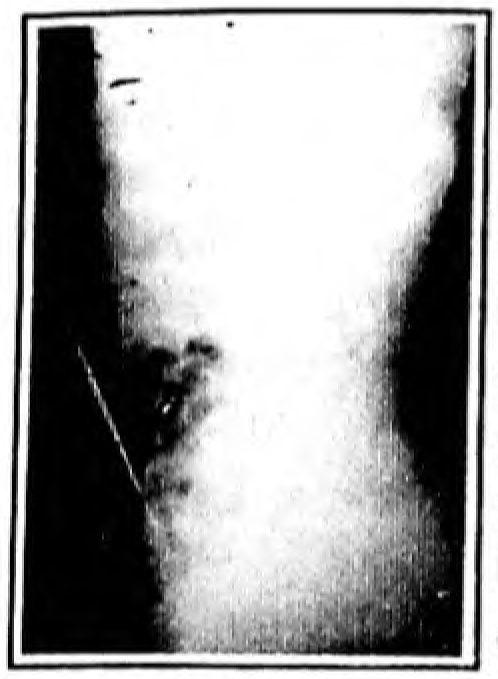


Fig-I

Discussion:

Iatrogenic foreign bodies are well known while most of these cause symptoms referable to the area of foreign body residence, usually within short span of time but iatrogenic abdominal foreign body remaining silent for long period is rare[1,2]. Our patient is unique in the sense that backache and radicular pain right lower limb brought her to the doctor and foreign bodies were incidentally discovered on X-ray. It is possible that perforation of part of IUCD occured while attempting its insertion[3,4]. When it was removed, patient became pregnant and dilatation and curreattage was performed, the time when currette might have entered the abdominal cavity. After D&C she was asymptomatic for 1½ year which is unusual. However it points that extreme caution needs to be taken by all persons dealing with IUCD insertion removal and D&C so that such mishaps will not occur in future.

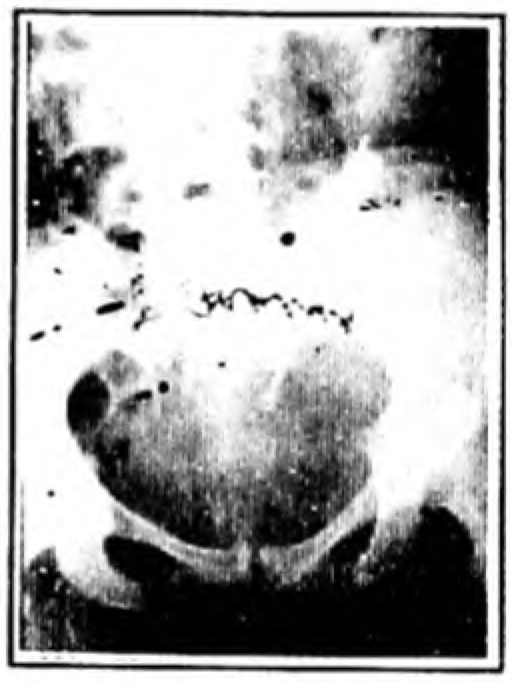


Fig-II

References:

1. Chandra S. and Sachdev S.K., perforation of Uterus. The journal of Obstetrics and Gynaecology of India, 401-405, Vol. XXXVII, June 1987 No.3.
2. Tietze C and Lewet S. Clin. Obstet. and Gynaecology 1971; 14: 4, 1317-35.
3. Tatum M. J: New York Population Council June 1970.
4. Timonen, H, Lukaimen, T, Raino, J and Ratum, H. Contraception, 1972; 6: 513.

From the Department of Gynaecology and Obstetrics Lala Ded Hospital & Govt. Medical College Srinagar. (Parveen, Bilquees, Farhat)

Received January 1999, Accepted March 1999

Correspondence: Dr. Parveen Malik, Senior Registrar L.D. Hospital, Srinagar, Govt. Medical College Srinagar J&K (India)

PATIENT WITH COUGH, FEVER AND PALPITATIONS

Riyaz Bashir MD; Tanveer Mir FACP

A 64-year-old Hispanic female from El-Salvador was referred to our hospital with one month history of dry cough, fever usually in the evenings and bilateral perihilar and upper lobe infiltrate on chest roentgenogram. A ten-day of treatment with Biaxin showed no response. She also complained of mild shortness of breath with occasional palpitations for last two weeks. Denied any history of weight loss, anorexia, night sweats, rigors, chills or chest pain.

Medical history:

Unremarkable.

Medications:

Biaxin for 10 days

Family history:

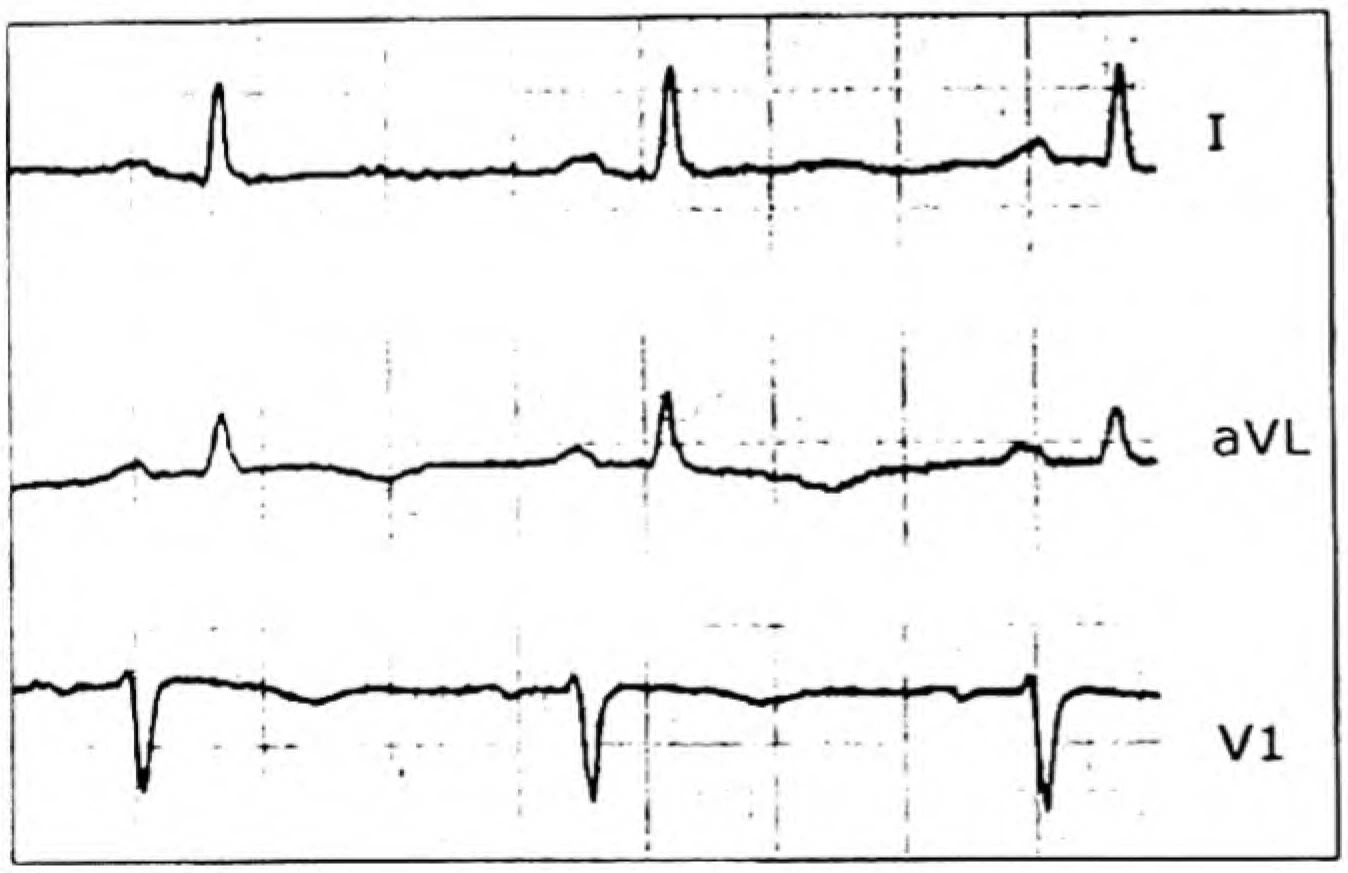
Non contributory (No contact with a known case of Tuberculosis).

Social history:

Married with three children. Denied any history of smoking or alcohol use. Husband gave up smoking 15 years ago.

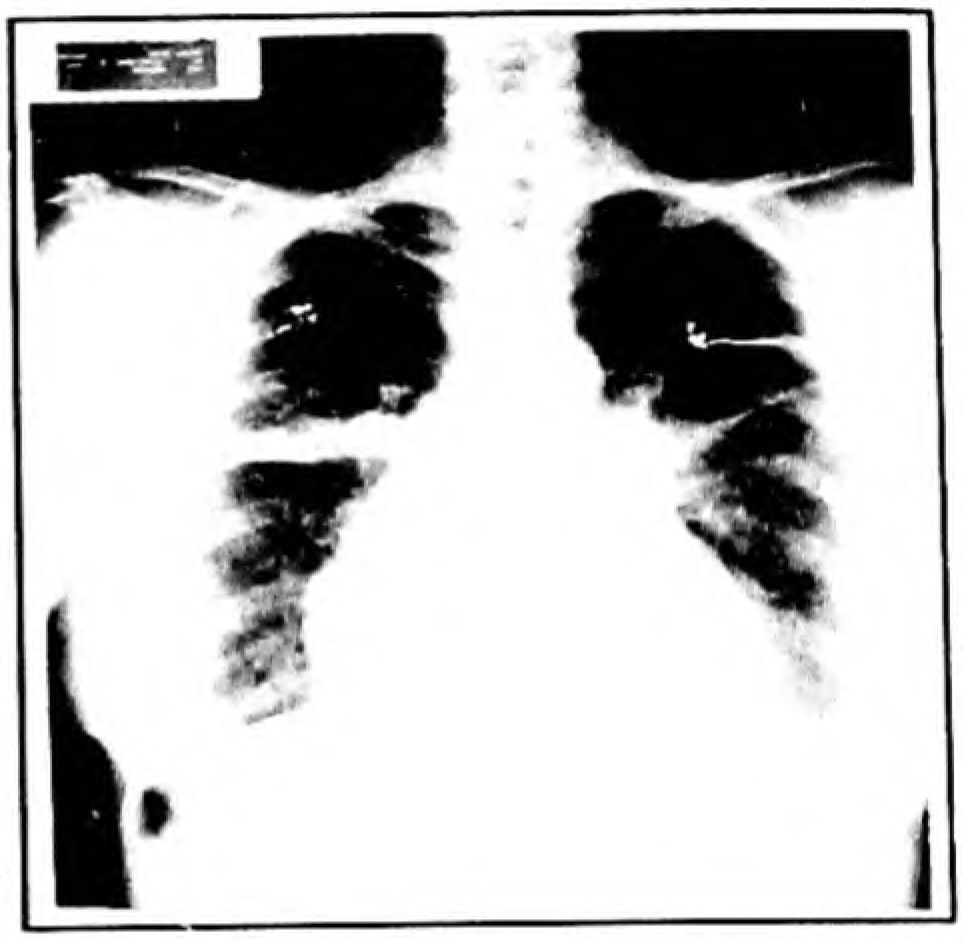
Travel History:

She had been in United States for last 6 years. Her last visit to EL Salvador was one year ago.



Physical examination:

Well-nourished, average built female in no apparent distress. She was alert and well oriented. Her temperature was 99°F, pulse 89 bpm, and respiratory rate of 18 breaths per minute, Blood Pressure was 150/80 mm Hg. There was no jugular venous distension noted nor was any pulsus paradoxus. No pallor, jaundice, lymphadenopathy or clubbing was noted. Trachea was central and chest and cardiovascular examination was normal. CNS, abdomen, breast, fundus, rectal and pelvic examinations were all normal.



Differential diagnosis:

Tuberculosis, Bronchogenic carcinoma, Lymphoma and Sarcoidosis.

Lab findings:

Renal profile and Calcium were within normal range. Hemoglobin was 13.7mg/dl, hematocrit was 40, WBC were 9,400/mm^3, with 81 per cent neutrophils, 9 per cent lymphocytes, 7 per cent monocytes and 3 per cent eosinophils. Platelet count was also normal. ESR was 67mm in first hour. PT and PTT were normal. Arterial gas revealed PaO_2 of 80 mmHg, $PaCO_2$ of 34 mmHg and pH of 8.43. Blood cultures, viral and fungal studies were also negative. PPD reaction was 12mm. Sputum AFB was negative. FANA was negative

JK-Practitioner 1999; 6(2): 151-152
From the Geriatrics Department of Medicine, Nassau County Medical Center (Mir, Bashir)
Received December 1998 Accepted March 1999

Correspondence to : Tanveer Mir, Associated Program Director, Chief Division of Geriatrics, Department of Medicine
Nassau County Medical Center 2201, Hempstead Tpke East Meadow, NY 11554 (USA)

Electrocardiogram is shown (Fig.1). Chest radiograph revealed bilateral perihilar and upper lobe infiltrates (Fig.2).

Hospital course:

Patient was started on cefuraxime. She developed an episode of palpitation at which time electrocardiogram showed transient atrial fibrillation. An immediate echocardiography was done which revealed a massive pericardial effusion with right atrial collapse. A pericardial window was performed and 1 liter of bloody fluid was drained. The cytopathological report showed a reactive inflammation with no evidence of tubercular process. CT scan revealed mediastinal lymphadenopathy and large pericardial effusion. Bronchoscopy with transbronchial biopsy was done which revealed adenocarcinoma.

Final diagnosis:

Adenocarcinoma of Lung with massive percardial effusion.

Outcome:

She received both chemotherapy and radiation therapy and was found to have a metastasis to radial bone. Patient died after 2 months due to recurrence of cardiac tamponade at which time she refused any invasive procedure.

Case breaker:

Echocardiography revealed massive pericardial effusion and definitive diagnosis was made by Bronchoscopy.

Key point:

1. Malignant pericardial effusion (MPE) is a common complication of malignancies, however it is rarely the initial presentation.
2. Malignant pericardial effusion is often large and rapidly accumulates with significant risk of tamponade. Later being the most common manifestation of metastatic cardiac involvement.
3. Etiologically more than two thirds of malignant pericardial effusions are caused by lung cancers and more than two thirds of these cancers are adenocarcinomas[1].
4. A narrow area in the aortic root carries all the lymphatic drainage from the heart and pericardium, hence the malignant involvement of this arrea causes massive pericardial effusion along with the retrograde lymphatic spread of malignant cells[2].
5. The most common presenting symptoms in these patients are cough and dyspnea. Most of these effusions are not recognized at the time of admission and sometimes the only clue to this complication may be low voltages on electrocardiogram as was the case in our patient.
6. The suspected or proven cases of tamponade are best treated by pericardiocentesis because emergent drainage procedure or window requiring general anesthesia is dangerous and should be avoided.
7. Pericardiocentesis alone is inadequate as recurrence rate is 90% within 90 days.
8. The definitive methods to control MPE are as follows[3]:
   a) Pericardiocentesis with sclerotherapy using doxycyline or Bleomycin (Efficacy at 90 days is 75%).
   b) Thoracotomy with pericardial window (Efficacy at 90 days is 90%).
   c) Video assisted thoracoscopy with pericardial window (Efficacy at 90 days is 95%).
9. Malignant pericardial effusion is associated with very poor prognosis, mean survival after the onset of symptoms is 19 weeks.

References:

1. Fincher RE. Malignant pericardial effusion as the initial manifestation of Malignancy. AM J Med Sci 1993; 305(2): 106-110.
2. Fraser RS, Viloria JB, Wang N. Cardiac tamponade as a presentation of extracardiac malignancy. Cancer 1980; 45: 1697-1704.
3. DeCamp MM, Mentzer SJ, Swanson SJ, Sugarbaker DJ. Malignant effusive disease of the pleura and pericardium. Chest 1997; 112: 291s-295s.

PHARMACOKINETICS OF DIACETYL MONOXIME (DAM) AFTER INTRAVENOUS ADMINISTRATION IN HEALTHY AND DICHLORVOS INTOXICATED COW CALVES

Sultana M; Srivastava A.K.

Abstract: *The pharmacokinetics of Diacetyl monoxime (DAM) have been studied in healthy dichlorvos (30 mg/kg. p.o.) intoxicated cross bred cow calves receiving an intravenous dose of 30 mg/kg. The distribution half life, elimination half life and apparent volume of distribution in healthy subjects were 0.83+0.01 h, 5.31+0.58 h and 1.04+0.09 L/kg, respectively, while in dichlorvos intoxicated animals the apparent volume of distribution was 0.47+0.04 L/kg, Half lives of distribution and elimination were 0.517+0.02 and 9.66+1.11 h, respectively. The results indicate that the kinetic behaviour of DAM gets altered in diseased conditions. The drug remains for a longer period of time in the body in poisoned animals than in healthy ones.*

Key words: *Diacetyl Monoxime, Dichlorvos; Pharmaco Kinetics; Insecticide; Organophosphorus*

JK-Practitioner 1999; 6(2): 153-154

Introduction

Diacetyl monoxime (DAM) is the standard antidote against organophosphate insecticides due to its ability to reactivate inhibited acetyl cholinesterase. It posesses greater central activity than 2-PAM (Taylor, 1980, Raina et al 1992). The efficacy of DAM is determined by its levels in blood and target tissue. As the information regarding the disposition kinetics of DAM in cow calves is either completely lacking or not sufficient attempts have been made to study the dispostion kinetics of DAM in healthy and dichlorvos intoxicated cow calves so as to determine the alteration of Pharmacokinetic parameters in intoxicated subjects.

Materials and Methods

Twelve (12) male cross bred cow calves (8-12 months of age) were randomly divided into two groups. The first group received DAM (Loba Chemie Indoaustranal Co. Bombay) at the rate of 30 mg/kg body weight by intravenous route. The second group received Dichlorvos (Vapona, 76% National Organic Chemical Industries Ltd.) @ 30 mg/kg body weight which was dissolved in 100 ml of tap water and drenched. DAM (30mg/kg body weight) was administered I.V. after appearance of severe toxic symptoms. Blood samples were taken from Jugular vein into heparinized test tubes before and at 1, 2.5, 5, 7.5, 10, 15, 30, 45, 60 min. 2, 3, 4, 6, 8, 10, 12, 24 h after injection of drug. Plasma was separated after centrifugation at room temperature.

Analytical Procedure

The plasma concentrations of DAM were determined as per the method of Dultz et al (1957).

Results and Discussion

The concentration - time profile of DAM administered i.v. to cow calves fit in a two compartment open model with first order distribution and elimination (Fig.1).

$$CP = A\,e^{-\alpha t} + B\,e^{-\beta t}$$

Where cp is the concentration of drug in plasma, A and B are zero time intercepts of initial and terminal phases of the concentration, α and β are the distribution and elimnation rate constants respectively and e represents the base of natural logarithm.

At 1 min. following i.v. administration of DAM (30 mg/kg) the peak plasma concentration reached the level of (96.9±0.72 ug/ml). The $t/2\alpha$ was 0.083± 0.01 h. DAM was rapidly transferred from central to peripheral compartment than from peripheral to central compartment. Various pharmacokinetic parameters of DAM are given in table 1. The apparent volume of distribution was 1.0± 0.09 L/kg. The $t/2\beta$ and ClB was seen to be 5.31±0.58 h and 137.4±7.17 ml/kg/h. The calculated value of volume of distribution (Vd area) was 1.04±0.09 L/kg and T/P ratio 2.90±0.30 indicated that DAM has extensive penetration into various body tissues and fluids. The longer value of elimination half life (5.31±0.58h) suggests that DAM is slowly eliminated from the body. Similar type of results were obtained by Srivastava and Malik (1986).

To investigate whether the kinetics of DAM is altered in Dichlorvos (OPI) intoxicated animals or not, the

---

From the Department of Pharmacology and Toxicology F.V.Sc. & A.H. Shuhama (SKUAST), Shalimar, Srinagar (Sultana) **and Deptt. of Pharmacolgy & Toxicology P.A.U. Ludiana, India.**

Received June 1998 Accepted February 1999

Correspondence to : M.Sultana, Assitant Professor, Deptt. of Pharmacology & Toxicology F.V.Sc. & A.H.Shuhama (SKUAST), Shalimar P.Box 1310, GPO, Srinagar

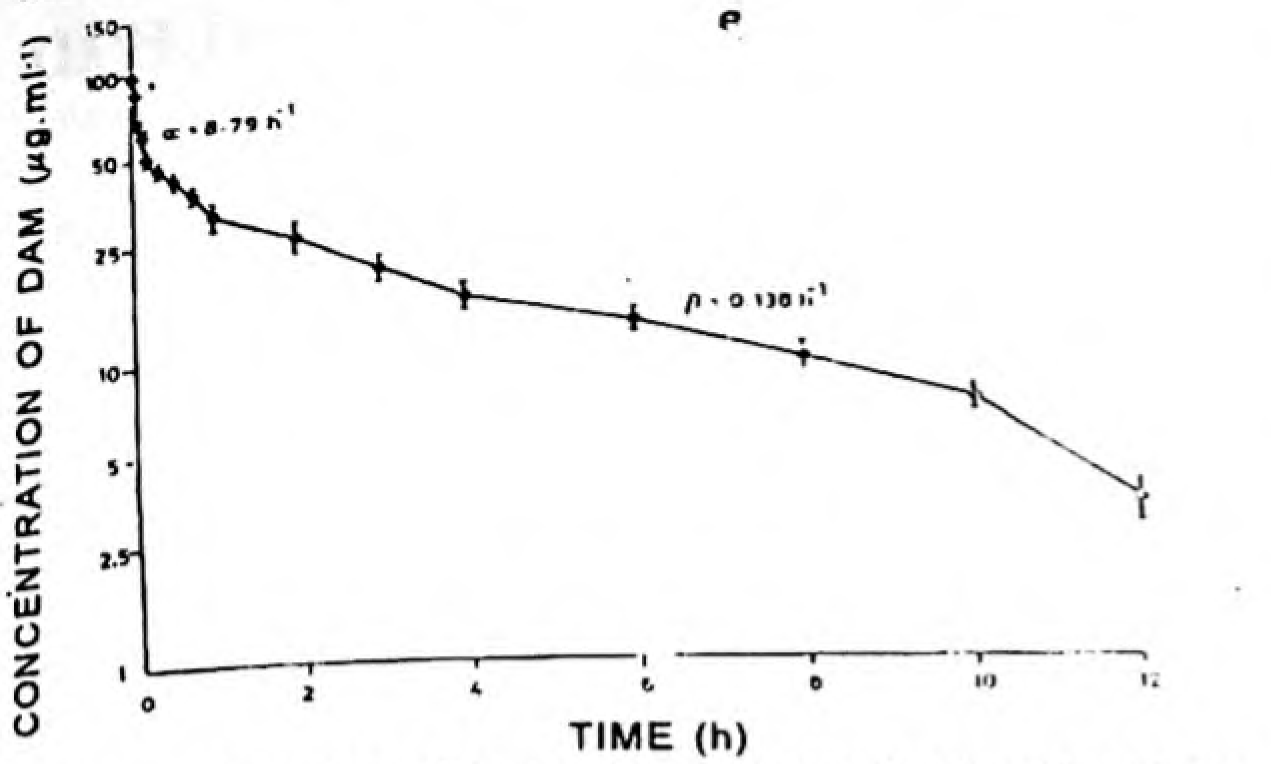


Fig.1. A semilogarithmic plot of plasma levels of DAM after a single iv dose of 30 mg/kg^{-1} body weight in cow calves. Values given are mean±SE of 6 animals

disposition kinetics of DAM was evaluated in dichlorvos (30 mg/kg, po) intoxicated cow calves. The mean plasma levels of DAM in intoxicated animals is shown in Fig.2. The peak plasma concentration (115.7±2.59 ug/ml) was observed at 1 min. which declined at 30 min. The data is best fitted in two compartment open model. The pharmacokinetic parameters based on its plasma concentration were calculated and are given in table 2. The distribution and elimination rate constant were calculated as 0.517±0.02 and 9.66± 1.11 h, respectively. On comparing the elimination kinetics it was found the t/2 B was markedly increased in poisoned animals as compared to healthy subjects. The value of Kel was lower in poisoned animals than in healthy subjects (0.17±0.01 h) and the mean residential time (MRT) of DAM was increased from 7.30 h in healthy animals to 13.03 h in poisoned animals. The results indicate that the kinetic parameters of both distribution and elimination got altered in dichlorvos intoxicated animals as compared to healthy subjects.

Table 1

Disposition kinetics of DAM in cow calves following a single intravenous dose of 30 mg/kg body weight.

Kinetic Parameters	Unit	Mean± S.E.
Cp°	**ug/ml**	113.4±3.13
t/2α	**h**	0.083±0.01
Vd (area)	**L/kg**	1.04±0.09
AUC	**ug/ml*h**	221.3±11.83
t/2β	**h**	5.31±0.58
Kel	**/h**	0.52±0.02
MRT	**h**	7.30±0.77
CIB	**ml/kg/h**	137.4±7.17
T/P	**Ratio**	2.90±0.30

The kinetic parameters are described as by Gibaldi and Perrier (1982).

The values are mean of six animals.

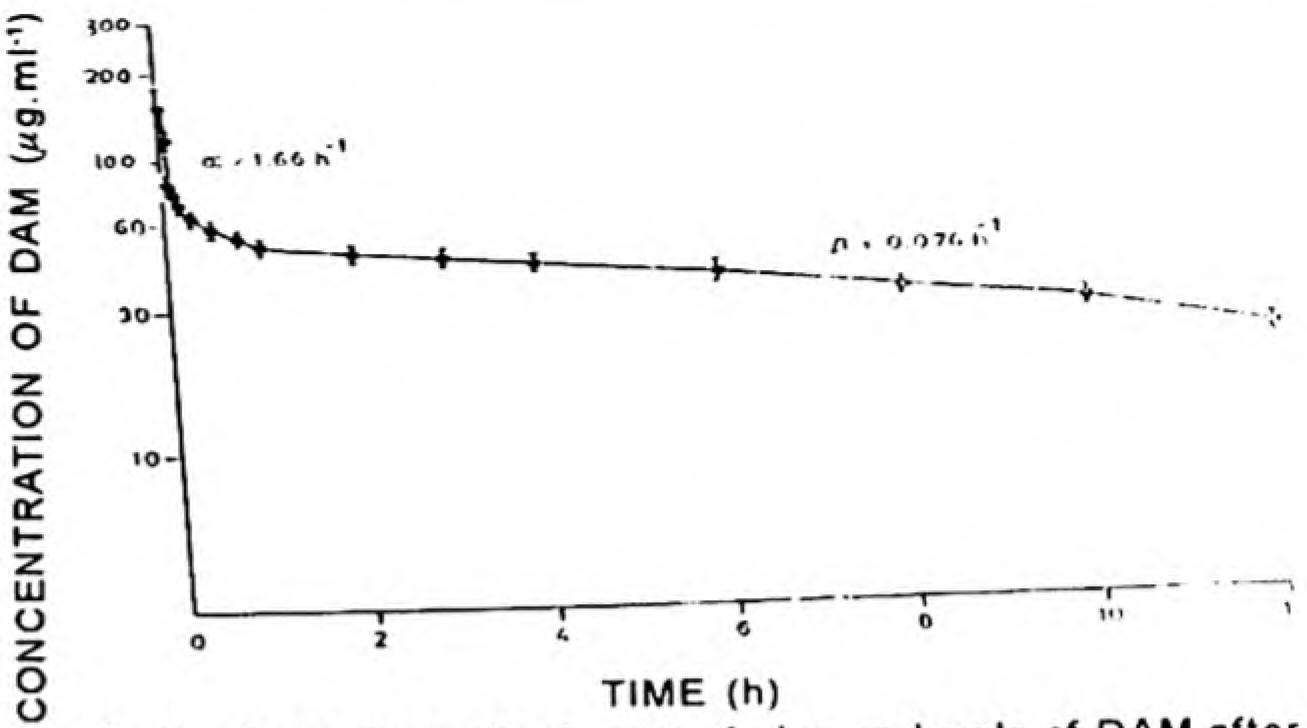


Fig.2. A semilogarithmic plot of plasma levels of DAM after a single iv dose of 30 mg.kg^{-1} body weight in cow calves, in which dichlorvos toxicity was induced with its single oral administration (30 mg.kg^{-1}). Values given are mean±SE of 6 animals

Table 2

Disposition kinetics of DAM in cow calves intoxicated with dichlorvos (30 mg/kg, po) and subsequently treated with single intravenous dose of DAM (30 mg/kg).

Kinetic Parameters	Unit	Mean± S.E.
Cp°	ug/ml	145.2±6.15
t/2α	h	0.517±0.02
Vd (area)	L/kg	0.47±0.04
AUC	ug/mlh	886.5±41.2
t/2β	h	9.66±1.11
Kel	/h	0.17±0.01
MRT	h	13.03±1.54
CIB	ml/kg/h	34.2±1.59
T/P	Ratio	1.22±0.08

The kinetic parameters are described as by Gibaldi and Perrier (1982).

The values are mean of six animals.

Acknowledgement

The financial help by Council of scientific and Industrial Research in the form of SRF, CSIR fellowship is greatly acknowledged.

References:

1. Dultz, L., Epsteim, M.A. Free-man, G., Gary, E.H. and Well, W.B. 1957. Studies on a group of oximes as therapeutic compounds in serin poisoning. J. Pharmacol. Exp. Ther. 119: 522-531.
2. Gibaldi, M. and perrier, D. 1982. Pharmacokinetics 2nd end. Marcel and Dekken, Inc. New York.
3. Raina, R., Srivastava, A.K., Malik, J.K. 1992. The influence of 2,3 butanedione monoxime on dichlorvos induced enzymatic changes in Buffalo calves. Vet. Hum. Toxicol. 34(3): 281-285.
4. Srivastava, A.K. and Malik, J.K. 1986. Pharmacokinetics and biochemical effects of DAM in Bubalus bubalis. Acta Veterinaria Hungarica 34 (3/4): 231-238.
5. Taylor, P. 1980. Anti Cholinesterase agents, In A.G. Gilman, L.S., Goodman and A. Gilman (eds) Goodman and Gilman's. The Pharmacological Basis ofTherapeuties 6th ed. Macmillan Pub. Co. Inc., New York, pp. 110-112.

ADRENAL INSUFFICIENCY IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODY SYNDROME-A REVIEW OF LITERATURE

Basharat Hussain Shah MD; Showkat Bashir MD; Tanveer Mir MD. FACP.

During the past few years there have been increasing reports of the association of adrenal insufficiency in patients with antiphospholipid antibody syndrome[1,2]. The pathogenesis, although quite uncertain is probably due to adrenal haemorrhage caused by adrenal vein thrombosis. Infarction secondary to thrombotic occlusion of adrenal vein has been confirmed on CT as well as on autopsy thus emphasizing the importance of recognizing adrenal failure in patients with antiphospholipid antibodies.

Antiphospholipid antibody syndrome is a thrombophilic disorder in which venous or arterial thrombosis or both may occur. It may occur in two forms-primary or secondary. In primary form there is a combination of recurrent thrombosis with serological evidence of anticardiolipin antibody or lupus anticoagulant or both. The secondary form is usually associated with, systemic lupus erythematosus, other connective tissue disorders, autoimmune disorders and certain lymphomas. Antiphospholipid antibodies are immunoglobulin directed against anionic phospholipid components of individual clotting factors resulting in increasing partial thromboplastin time (PTT) which is not correctable by the addition of normal plasma. These antibodies include anticardiolipin antibody, lupus anticoagulant and an antibody implicated in false-positive VDRL. The clinical syndromes of vaso-occlusive disorders associated with antiphospholipid antibodies namely lupus anticoagulant thrombosis syndrome and anticardiolipin antibody thrombosis syndrome have been identified to be caused by immune-mediated disruption of endothelial function. This syndrome encompasses arterial and venous thrombosis, episodic thrombocytopenia, recurrent fetal loss after first trimester, premature baby, placental thrombosis/infarction, neurological dysfunction (migraine, chorea, encephalopathy) systemic and pulmonary hypertension and endocardial disease[3].

Adrenal and renal vein thrombosis in patients with antiphospholipid syndrome have been described in literature[4,5,6]. They can present with adrenal insufficiency or rarely addisonian crisis in patients with adrenal vein thrombosis or intractable hypertension in patients with renal vein thrombosis. The concomitant adrenal haemorrhage and renal artery thrombosis can sometimes mimic pheochromocytoma clinically[6]. The thrombosis of adrenal vein, although rare, can occur in patients who, in the presence of underlying stress along with coagulopathy are at increased risk for bilateral adrenal haemorrhage (BAH) leading to adrenal insufficiency. The symptoms of adrenal haemorrhage although nonspecific, include chest, back, flank or abdominal pain usually associated with fever. Hypotension is frequently a preterminal finding. Biochemical evidence of adrenal insufficiency such as hyponatremia, hyperkalemia, leukocytosis, acidosis and azotemia are common. A sudden decrease in hemoglobin or hematocrit, although rare, can occur at the time of adrenal haemorrhage. Hence the physician should have high index of suspicion in those patients who are at high risk and recognize nonspecific manifestation of adrenal insufficiency. Once the diagnosis is established prompt steriod replacement can be life saving.

The anatomic diagnosis can be established by CT scan of abdomen after which hormonal function can be evaluated with a rapid corticotropin stimulation test[6]. Concomitant single base line plasma sample shows low cortisol. High corticotropin levels can be obtained as an alternative to rapid corticotropin test as long as steriod replacement is not inordinately delayed and patient is hemodynamically stable[6]. In brief, an acute medical or surgical stress along with a hypercoagulable state are risk factors for bilateral adrenal haemorrhage. The presence of circulating lupus anticoagulant is probably an additional contributing factor. A heightened awareness of adrenal haemorrhage should result in increased

---

JK-Practitioner 1999; 6(2): 155-156

From the Department of Medicine, Geriatrics Division (Shah, Bashir, Mir) **Nassau County Medical Centre, East Meadow, NY11554 USA**

Received December 1998 Accepted February 1999

Correspondence to : Dr. Tanveer Mir, MD,FACP; Associate Program Director, Chief Division of Geriatrics, Nassau County Medical Centre, State University of New York at Stony Brook, 2201 Hempsted Turnpike, East Meadow, New York 11554, USA

antemortem recognition, treatment and improved survival.

References:

1. Asherson RA, Hughes GRV: Recurrent deep vein thrombosis and Addisons disease in primary antiphospholipid syndrome. J Rheumatol 1989; 16: 378-80.
2. Waiz B, Kong HPP, Silver R: Adrenal failure and primary antiphospholipid syndrome. J Rheumatol 1990; 17: 836-7.
3. McGee SG, Pearce HW, Sharma L, Gree D, Yao S.T: Antiphospholipid antibody and arterial thrombosis. Arch Surgery 1992; 127: 342-46.
4. Siu B.C.S. Kitzman W.D. Sheedy FP, Northcutt CR: Adrenal insufficiency from bilateral haemorrhage-Mayo clinic Proc 1990; 65: 664-670.
5. Asherson AR, Hughes RGV: Hypoadrenalism Addison's disease and antiphosoholipid antibodies J Rheumatol 1991; 18:1.
6. Rao RH, Vagmicci AH, Amico JA: Bilateral massive adrenal haemorrhage; early recognition and treatment. Ann Intern MEd 1989; 110: 227-35.

With Best Compliments From

Nira Sons

Chinar Trust Building, Maulana Azad Road, Srinagar-190001

DISTRIBUTORS FOR:

☐ **Hoechst Marion Roussell Ltd.**

☐ **German Remedies Ltd.**

☐ **Fulford India Ltd.**

☐ **S.G. Pharmaceuticals Ltd.**

☐ **Group Pharmaceuticals Ltd.**

☐ **Wockhardt Ltd.**

☐ **Searle India Ltd.**

☐ **Sarabhai Chemicals Ltd.**

☐ **Raptakos, Brett & Co. Ltd.**

ANTI-CANCER DRUGS AND ANTI-RABIES VACCINE AVAILABLE

THE INDIVDUAL VOLUMANORY AND STRUCTURAL VARIATIONS OF THE STOMACH DUE TO THE HOMEOSTASIS OF THE ORGANISM

V.I. Pivtorak

The main functions of the gastro-intestinal tract (G.I.T.) are digestion, excretion, protection and endocrinal. All these functions directly take part in the maintenance of the internal equilibrium of the body. The most important mechanism in maintaining the homeostasis is control of the entrance of foreign particles in the body. This is performed by the complex protective mechanism of the stomach. It consists of mechanical or passive factors (mucosae, epithelial cells, peristalsis, HCl, peptidase), factors of non specific resistance (digestive leucocytis, phagocytosis, transferins and other proteins) and the autonomous immune system. Due to this complex system the harmful part of our diet is effectively neutralised. It protects the body from microorganism which are present in the food. Important role in maintaining the internal balance is played by the excretion of metabolites from the body.

The aim of this work is to study the interrelationship and the importance of morphological and functional changes of the stomach.

Material and Methods used

The topographico-anatomical analysis of the interrelationship between the organs of the abdominal cavity was carried out with the help of CAT Scan on 133 patients under suspicion for disease of G.I.T. For comparison a control group of 36 men and 16 women representing different age groups and constitutional conditions was made, even the CAT scans of patients not suffering from gastric and duodenal diseases were used. Before the CAT scaning of the patients their constitutional status was determined keeping into consideration, their sex and body structure. Dolychomorphous, brachiomorphous and mesomorphous type of body structure was determined taking into account the shape of the thorax, the size of the costal angle and growth index in accordance with the recommendations of W.H.O. For the analysis of the tomogrames the system of topographico-anatomical co-ordinates of the human body was used.[1]

The initial material for the study of morphological and functional distinctions of normal and resected stomach was the material acquired during gastric biopsy done with the help of fibrotic gastroscope. The material was fixed with 10% neutral formalin and immersed in paraffin. The sections were stained with the help of haemotoxilin-eosin and according to Van Heusen. For the identification of neutral and acidic mucopolysaccharides the SHIK-reaction and Hail-reaction were used. In some of the cases electron-microscopical analysis was carried out.

Results and Conclusions

The analysis of the CATscan showed that the vertical placement of the stomach corelates with the constitutional type of the person. Hence in people with brachiomorphical type of constitution the stomach is placed higher than others, and its anterior projection is usually in the shape of a horn. In people with dolychomorphic type of constitution the stomach is placed lower and its anterior projection is in the shape of a hook. The interdependence of the size of the retrogastric space with the constitution of the person was found[2]. The minimal size of the retrogsatric space at the cardiac, central and the antral sections of the stomach was found in people with dolychomorphic, the average in people with mesomorphic and maximum in people with brachiomorphic type of constitution. This agrees with the results of E. Schultz[3].

Dumping syndrome (post cibal syndrome) in our view can be referred to the disorders caused due to the disruption of homeostasis of the food in the duodenum. This syndrome usually occurs in patients who have undergone resection of the stomach and due to the exclusion of duodenum from the process of equilization of the concentration of the ingredients in the enteral environment to the levels close to that in the blood. In these patients postoperatively food from the stomach goes directly to the jejunum, which leads to improper absorption of the nutrients. This leads to the imbalance

JK-Practitioner 1999; 6(2): 157-158

From the Department of Operative Surgery and Topographical Anatomy (Pivtorak)

Received November 1998 Accepted March 1999

Correspondence to : Dr. V.I.Pivtorak, Asstt. Professor Operative.Surgery and Topographical Anatomy Vinnitsa State Medical University n.a. N.I.Pirogov, Ukraine

of the nutritive homeostasis and the development of the characteristic clinical picture.

The endocine cells of the digestive tract secrete more than 30 peptide hormones which not only control the basic functions of the G.I.T. but also coordinate the different aspects of the complex process of digestion and absorption of food[1]. Some of these digestive hormones have multiple origins and functions. They not only act as hormones but also as neurotransmitters. These include vasoactive intestinal peptide (VIP) cholycystokinine, gastrin etc.

The study of the endocrine apparatus of the stomach shows a considerable participation of the cells of diffuse endocrine system in compensatory and adaptive processes, linked with development of illnesses (gastritis, peptic ulcer). Hyperplasia of the endocrine cells was seen during atrophic changes of the mucosae. It is possible that this hyperplasia is a compensatory reaction to the inflammation and the atrophic changes, at the same time we can not exclude the trophic effect of the peptic hormones and the bioactive amines.

Due to weakning of the protective barrier the risk of infiltration of viruses, bacteria and other infectious diseases increases. Nowadays it is well known that infection through the G.I.T. causes not only acute but also chronic diseases of the stomach, intestine, liver and other systems. The mucus membrane and the epithelium of the G.I.T. is not an absolute barrier even in healthy adults because there is always a possibility for the penetration of antigens. Many toxins formed due to digestion of food, metabolic products of microorganisms, digested and partially digested proteins and bioactive substances enter the blood along with the nutrients. Their amount is usually not large enough to disrupt the homeostasis, but in some cases their amount might increase and reach critical levels. These situations usually arise in children, because their G.I.T. is not fully developed and the permeability of the mucosae is high for macromolecules. This is the main reason for the development of alimentary allergies. In adults the increased influx of proteins in the body may be due to genetic inadequacy of the given system, high protein intake, intoxication, carcinogens, and alcohol. The protective function of the digestive system in case of damage to internal organs has not been extensively studied.

After the above study we come to the conclusion that G.I.T. takes part in many processes which maintain the homeostasis like-protection, digestion, regulation of appetite, endocrinal regulation and excretion of metabolise. The disruption of any one of these mechanisms causes the infiltration of living and nonliving antigens which cause the increased intake of some and decreased intake of other nutrients, disturbance in the hormonal regulation of the organism and the retention of metabolic waste in the blood. All this may be the cause of disruption of homeostasis and development of diseases of internal organs. The retention of metabolites in the organism worsen the course of illness and lowers the effectiveness of the treatment.

In this way the digestive tract consists of mechanisms which take part in maintaining the internal balance of the organism. Disruption of these processes cause the development of pathological processes or their chronication but this needs further study.

References:

1. Bourych M.P. Integrative geotopographic approach to the study of the human structure. Reports of Morphology 1996; Vol. 2, N 1. 22-26.
2. Pivtorak V.I. Computer-tomographical reconstruction of the stomach/Reports of Morphology 1997, Vol.2, N 3. 36-37.
3. Schultz E. Measurements of the retrogastric space/ Radiology. 1965- Vol. 84, N 1. S. 58-65.
4. Sarker S. A., Gyr K. Non-immunological defence mechanisms of the gut. Gut-1992; Vol. 33, N 7. P. 987-993.

Hepato-Biliary & Pancreatic Ascariasis in Endemic Areas

Ascariasis is endemic in Indian and many developing countries, however, impact of this ubiquitous parasite on human health had never been quantified. In fact this human infection had been identified as benign without any major potential for disease.

Over the years (1982-1995), I and my colleagues got interested in public health importance of this human infection. In an endemic area in Kashmir, we identified that the commonest manifestation of this infection was due to peculiar but natural behaviour of this large motile organism to explore human orifices, this time, papillary orifice of the bile and pancreatic ducts. In doing so, the hepato-biliary and pancreatic ducts are freely traversed. The Ascarides make repeated visits into and out of the ducts till at some stage of the travel die in the duct (death dance of the biliary demon). During its repeated but limited exploration of papillary orifice and advance into ducts, the person comes down with severe hepato-biliary or pancreatic disease, the nature of which is predictably defined by the numbers and placement of the Ascarides in the ducts. We have named this disease as Hepatobiliary and Pancreatic Ascariasis (HPA). The dead Ascarides in the ducts forms a nidus to the formation of brown pigment stones, leading to the syndrome of Recurrent Pyogenic Cholangitis, a disease more often known in the Orient as Oriental Cholangiohepatitis.

HPA is a disease of great public health importance in endemic areas. In Kashmir, one such area, HPA is as common as gall stones in causing biliary disease and every third patient with acute pancreatitis is caused by HPA. HPA is only second to bleeding peptic ulcer as a cause of emergency room visits. Moreover, around 12.5% of all biliary lithiasis are caused by primary brown pigment stones, placed in hepatic ducts and are secondary to aftermath of repeated Ascaris invasion into ducts.

The data on epidemiology, clinical picture, diagnostic tools, management strategies including therapeutic endoscopic interventions and of course control measures have been collected in a series of carefully planned studies and formed a series of important publications (see references overleaf).

In view of the frequent international travel and emigration of eastern population to the West, HPA can be frequently encountered by the western physicians dealing with high risk population or those who have had recent travel to endemic zones.

M.S. Khuroo
DM, FACP, FRCP (Edin)
Consultant Hepatology Head, Section Gastroenterology
Dept. Medicine (MBC 46)
King Faisal Specialist Hospital & Research Centre
PO Box 3354 Riyadh 11211
Tel/Fax: (966-1) 442-6202 e-mail:khuroo@kfshrc,edu.sa.

JK-Practitioner 1999; 6(2):159

References:

1. Khuroo MS, Zargar SA: Biliary ascariasis: a common cause of biliary and pancreatic disease in an endemic area. Gastroenterology 88: 418, 1985.
2. Khuroo MS, Zargar SA, Mahajan R, et al: Sonographic appearances in biliary ascariasis. Gastreonterology 93:267, 1987.
3. Zargar SA, Khuroo MS: Treatment of biliary ascariasis and its rationale. Gastroenterology 93:668, 1987.
4. Bushan B, Watal G, Majahan R, et al: Endoscopic retrograde cholangiopancreatographic features of pancreatobiliary ascariasis. Gastrointest Radiology 13: 327, 1988.
5. Khuroo MS, Mahajan R, Zargar SA, et al: Biliary and pancreatic ascariasis: a long-term follow-up. Nat Med J India 2:4,1989.
6. Khuroo MS, Mahajan R, Zargar SA, et al: Prevalence ob biliary tract disease in India: a sonographic study in adult population in Kashmir. Gut 30:201, 1989.
7. Khuroo MS, Mahajan R, Zargar SA, et al: Endoscopic vs surgical drainage of biliary tract in acute pyogenic cholangitis: a controlled study. Indian J Gastroenterol 8:119,1989.
8. Khuroo MS, Zargar SA, Majahan R: Hepatobiliary and pancreatic ascariasis in India. Lancet 335:1503, 1990.
9. Zargar SA, Khuroo MS: Management of biliary ascariasis in children. Indian. J Gastroenterol 9:321, 1990.
10. Khuroo MS, Zargar SA, Yattoo GN, et al: Ascaris-induced acute pancreatitis. Brit J. Surg 79:1335, 1992.
11. Khuroo MS, Zargar SA, Yattoo GN, et al: Sonographic findings in gallbladder ascariasis. J Chin Ultrasound 20:587, 1992.
12. Khuroo MS, Dar MY, Yattoo GN, et al: Serial cholangiographic appearances in recurrent pyogenic cholangitis. Gastrointest Endosc 39:674, 1993.
13. Khuroo MS, Zargar SA, Yattoo GN, et al: Oddi's sphincter motor activity in patients with recurrent phyogenic cholangitis. Hepatology 17:53, 1993.
14. Khuroo MS, Zargar SA, Yattoo GN, et al: Worm extraction and biliary drainage in hepatobiliary and pancreatic ascariasis. Gastrointest Endosc 39:680, 1993.
15. Khuroo MS. Ascariasis. Gastroenterology Clinics of North America 1996; 25:553-77.

EUTHANASIA:- The Debate goes on

Fayaz A.Bhat, M.D.; G.M.Malik, M.D.; Zaffar Abbass, M.D.

There is a great deal of international debate and experimentation with euthanasia today from the practice of euthanasia in Holland, to anonymous reports of euthanasia in American Medical Journals, to citizens in States who are attempting to legalise euthanasia through refrendums, we are confronted with controversy surrounding euthanasia on a daily basis.

Euthanasia from Greek "an easy or happy death is defined as act of putting to death painlessly one who is suffering from an incurable disease or condition. Only because we now have the technical ability to delay indefinite by imminent death, do the problems of active and passive euthanasia or withdrawal of therapy arise. Withdrawal of therapy is now considered, under the appropriate circumstances" reasonable, humane and legal.

The Hippocratic Oath declares opposition to the practice of euthanasia. In 1988, the council on Ethical and Judicial Affairs of American Medical Association reaffirmed its opposition to euthanasia but the practice of euthanasia is being widely performed in Holland. The technique is to administer an hypnotic like barbiturate which is then followed by a lethal injection of a paralytic agent. It is estimated 5000 to 10,000 Dutch are euthanised each year.

In Holland, four criteria are used to determine its legitimacy.

1. The patient must be under severe mental and/or physical anguish, with no prospect of relief.
2. The patient must make the request freely, frequently, consistently, without coercion to the physician and physician may solicit the patient.
3. Assisted-death may not be an answer to pain, fear, failing care, or loneliness, further alternatives to euthanasia must be offered by the physician.
4. A colleague must be consulted by the primary physician to confirm the diagnosis and prognosis, the lack of other treatment options, and to ensure that all legal requirements for euthanasia have been met.

The view held in various European institutions, is that there is no real difference between withdrawal of life-supporting measures and administration of agents that will result in the cessation of all organ function. Both acts will lead to death. However, withdrawal of life support might bring discomfort to the patient and prolong an arguably useless agony. On the otherhand, a pharmacologic intervention that can hasten an ongoing dying process will avoid suffering, indignity and costs associated with prolonged terminal phase.

Ethical objections have been that there is a fundamental difference between the two attitudes since one can be seen as "Killing" and the other "Letting die". This difference, however, becomes meaningless in a particular environment where something can be done to support the failing body.

Nobody could argue that withdrawal of minimal support (i.e, fluids & nutrition) will result in death, exactly as increasing doses of sedating drugs will. But starving some one to death is felt to be unacceptable and unreligions by physicians, nurses as well as the public. In the context of dying patient in ICU, the precise definition of the means used to shorten the dying process is irrelevant provided the patient does not suffer withdrawal of mechanical ventilation is seldom performed because it might bring discomfort to the patient. Sometimes, mechanical ventilation could even be started in a dysneic patient before sedation is approved once the patient is relieved of dysnoea.

Inspite of the possible benefits of euthanasia it is to be both perilous as public policy and corrosive as medical practice. Also euthanasia could be used, in our present environment of cost-containment and social-injustice, as a means of "rationing" care. Euthanasia could have corrosive effect on the practice of medicine by detracting attention from other issue, such as need to improve pain control, patient-physician communication and care for the dying.

Physicians working in Critical Care Units are deadly opposed to participating in euthanasia. Physicians and Intensivists are clearly opposed and should not participate in euthanasia. There is great concern, euthanasia will expand from a practice which is desired by legally

JK-Practitioner 1999; 6(2): 160-163

From the Department of Medicine SKIMS, Soura Srinagar, India (Bhat) **and Department of Medicine** (Prof Malik) **and Pharmacology** (Abbas) **GMC, Srinagar India.**
Correspondence :Fayaz A. Bhat. Senior Resident Deptt. of Medicine SKIMS, Soura, Srinagar.

competent patient to something which is used by surrogats of legally incompetant patients and eventually as an act which might be used to terminate life at an earlier stage in patients who are in disadvantaged or vulnerable groups. Finally, euthanasia might strike a lethal blow at the heart of what it means to be a physician. The social and professional role of physicians as healers would be destroyed. Additionally, euthanasia is not consistent with the role of physician as healers who is committed to the sanctity of life. Death like birth, should remain a natural event of our everyday life. The right to die with dignity must remain a fundamental ethical principle.

Background Data

Access to and delivery of pain treatment and other palliative measures are seriously deficient in the present health care systems in the United States. Physician under-recognition and undertreatment of pain and depression in dying patients has been repeatedly shown, and most physicians have been inadequately trained to provide palliative care. Medical students and residents are not uniformly taught about pain relief, hospice care, and communication about death and dying, and less than 10% of internal medicine training programmes include supervision and treatment of dying patients who are receiving palliative care.

Fifty percent of patients who died had moderate to severe pain at least half of the time during their last 3 days of life. Solomon and colleagues showed that physicians frequently recognized that they were overtreating patients at the end of life but did not know how to stop.

Unrelieved or unrelievable pain is not often the major or sole reason for requests for physician-assisted death. Physicians report that unrelieved pain is infrequently the only reason cited by patients who request or receive physician-assisted suicide or voluntary active euthanasia. In the first Rmmelink study, unrelieved pain was the sole reason for euthanasia requests in 5% of cases, was part of the problem in 40%, and was not reported at all in the remaining 60% (the 5% of cases were included in the 40%). The most common reasons cited were intolerance of physical disintegration, dependence, being a burden, extreme fatigue, and lack of meaning. A study of the secret practices of Washington State physicians with respect of physician -assisted suicide showed similar results. Studies of patients who discontinue life support, such as dialysis, also show that unrelieved pain is not usually the sole motivating factor for discontinuation.

Some patients who request physician-assisted death have clinical depression, but others have no definable mental or cognitive impairment. The evaluation of depression in terminally ill patients is challenging because common symptoms of terminal illness overlap with symptoms of depression, such as fatigue, sleep distrubance, poor concentration, loss of interest in normal affairs, weight loss, and pre-occupation with death.

Extremes of otherwise unrelievable suffering can be managed by sedation too. Unconsciousness (terminal sedation), a practice that is gaining acceptance among palliative care groups but is not universally accepted. The prevalence of terminal sedation is unknown, and its acceptability to terminally ill patients, their families, their physicians, other health care providers, and society has yet to be demonstrated.

Public and professional opinion in the United Stats is deeply divided about physician-assisted suicide. Over the past 10 to 15 years, public opinion polls consistently show that two thirds to three fourths of the U.S. public support a more open and accessible practice of suicide. Physicians in the United States are much more reluctant to participate in voluntary active euthanasia than in physician-assisted suicide.

In our view, public opinion alone is not a rational basis for the legalization of physician-assisted suicide.

Despite legal prohibition, some patients request physician-assisted sucide and some physicians secretly provide it. Studies about physician-assisted death in the United States are based on physician self-reports of an illegal practice and are further limited by low response rates, poor generalizability, differing regional attitudes, and ambiguous question construction; thus, exact frequencies are uncertain. A survey of Washington State physicians showed that in 1 year, 12% of respondents received a request for physician-assisted suicide and 4% received a request for voluntary active euthanasia. Physicians acceded to approximately 25% of these requests. A study of physicians caring for patients with AIDS in San Francisco showed that closer to 50% of these physicians had participated in at least one case of physician-assisted sucide.

Terminal sedation is sometimes used to relieve suffering that cannot otherwise be satisfactorily controlled. The patient is sedated to unconsciousness, usually with barbiturates, opioids, or benzodiazepines. Life-sustaining therapy is then withheld so that the patient dies of dehydration or from complications of the underlying disease. The rate at which terminal sedation is used varies from 0% to 40%, depending on the clinical site. Some guidelines and safeguards for this practice have been proposed, but empirical data are lacking about the circumstances of its use and its acceptability to patients, families, or professional groups. Some instances of terminal sedation may be viewed as cases of "slow euthanasia".

Convergent Views

Forging a consensus about good care of the dying requires taking into account the background data outlined above. The common ground between the two sides of the physician-assisted suicide debate includes the following seven areas.

1. A central goal of medicine is to relieve suffering by helping people die with comfort, support, and meaning.
2. Comprehensive, interdisciplinary palliative care is the standard of care for persons with progressive, advanced disease for whom prognosis is limited and the focus of medical management is quality of life.
3. Physicians must provide adequate pain relief according to well-established standards.
4. Patients have the right to refuse unwanted treatment or to stop treatment once it has been started.
5. Patients who request that death be hastened-by the for going of life-sustaining therapy, the voluntary cessation of eating and drinking, terminal sedation, physician-assisted suicide, or active euthanasia-should have their requests fully explored, and they deserve an' exhaustive search for palliative alternatives. These requests should be viewed as a "cry for help," the meaning of which should be carefully explored.
6. Even if physician-assisted suicide is justified under some exceptional circmstances, this does not necessarily mean that it should be supported as public policy.
7. Every physician should remain committed to the skillful and compassionate care of the terminally ill throughout the dying process but should not be required to violate his or her own fundamental values.

Islamic Perspective

The sanctity of human life is ordained in the Qur'an (the holy book of Islam). "Do not take life which God had made sacred except in the course of Justice" and anyone who has killed a fellow human except in lieu of murder or mischief on earth, it would be as if thee slew the whole mankind."

About suicide, the Quran says, "Do not kill yourselves as God has been to you very merciful." Taking away the life should be the domain of the one who gives life. The Quran says, "Anyone who has saved a life, it is as if he has saved the life of whole mankind."

The Islamic Medical Association (IMA) endorses the stand that there is no place for euthanasia in medical management, under whatever name or form (e.g. mercy killing, suicide, assisted suicide, the right to die, etc.) Nor does it believe in the concept of a willful and free consent in this area. The mere existence of euthanasia as a legal and legitimate option is already pressure enough on the patient, who would correctly or incorrectly, read in the eyes of his/her family the silent appeal to go. At the same time, IMA holds the view that when the treatment becomes futile, it ceases to be mandatory. This would determine the utility of administration or continuation of medical treatment (including the respirator). Under such circumstances, the basic human rights of hydration, nutrition nursing and pain relief cannot be withheld. These may be carried at home or in an institution as the case warrants. The demarcation between futile and infutile medical treatment is often blurred. Proximity to death cannot define futility of treatment, since near-dead patients may often be successfully treated and revived. However this area remains open for research perhaps the relation of outcomes to a battery of clinical parameters, or combinations thereof, might help the establishment of a "futility index" with reasonable precision, that would further guide the current clinical assessment.

The IMA follows the current DNR (Do not resuscitate) policy, where treatment is deemed futile. Brain death including the brainstem, is an acceptable definition of death, with all the consequences. Pertaining to cessation of animation or the procurement of vital organs for transplantation. Emphasis in such patients should not be on primary disease but on quality of life such as controlling the accompanying symptoms like pain, weakness, excretory dysfunction, ulceration etc. Affective and psychological care is important, and both caregivers and family (guidelines or brief courses) should be trained for it.

The spiritual dimension should be recruited to help the patient. This is not the function of clergy only, but health professionals should have adequate training in handling patients and guiding families. Care of the terminally ill should not belong in "rush" medicine or hurried physicians.

Care givers should have an insight into the various religious, cultural and ethnic backgrounds pertaining to terminal illness and health. A book may be collated indicating culture-specific guidelines.

Since we live in a time when one's home is no more suitable to be born in or to die in, reliance has become heavy on institutional care, which tremendously pushes up the cost of the care.

Encourage,ment of volunteerism and perhaps providing incentives might cover part of this gap and is good for moral society at large.

Of course, the issue of care for terminally ill, as a component of health care in general, is closely combined with modern trends in restructuring health care. It is regrettable to see that the business aspects of health care are expanding at the expense of the service side of health care. A radical review is needed. It takes a society that is more human orientated than money oriented.

Further Reading:

1. Angell M: Euthanasia, N Engl J Med 1988; 138: 1000.
2. Back AL, Wallace JI, Starles HE etal. Physician assisted sucide and euthanasia in Washington State. Patient requests and physician responses JAMA 1996; 275: 919-25.
3. Baile WF, DiMaggio JR, Schapira DV etal. The request for assistance in dying. The need for psychiatric consultation- Cancer. 1993; 72: 2786-91.
4. Billings JA, Block S. Palliative Care in undergraduate education: Status report and future direction - JAMA. 1997; 278: 733-8.
5. Foley KM. Pain, Physician assisted suicide & euthanasia Pain Forum. 1995; 4: 163-78.
6. Medical Ethics Committee; Islamic Medical Association of North America. Care at the end of life and Euthanasia. JIMA 1997; 29: 100-101.
7. Raffini TA, Shurkins J, Sinkler WS: Intensive Care. Facing the Critical Choices. New York, Freeman, 1988.
8. Soloman MZ, O'Donnell L, Jennings B etal Decisions near the end of life: Professional, views on lifesustaining treatments Am J Public Health. 1993; 83: 14-23.
9. The Glorious Quran Chapter 4 verse 29, Chapter 6 verses 32, 37 & 151, Chapter 31 verse 17, chapter 39 verse 10.
10. Thomas A Raffin. Perspective on clinical Medical ethics in Hall BJ et.al Principals of Critical Care Medicine page 2185-2204.
11. Wanzer SH, Federman DD, Adelstein SJ, et al. The physicians responsibility toward hopelessly ill patients. A second look. N Engl J Med 1989; 320: 844.
12. Young EWD. Alpha & Omega: Ethics at the Frontiers of Life & Death. Palo Alto, Addision Wesley, 1988.
13. Quill ET., Meier ED., Block DS et al. The Debate over Physician-Assisted Suicide: Empirical date and Convergent views. Ann Int. Med. 1998; 128: 552-8.
14. Burt AR. The Supreme Court Speaks-Not assisted Sucide but a Constitutional right to palliative care. N. Engl J Med 1998; 337: 1234-36.

SUBSCRIBE

Subscription Rates
(India) in Rupees

	1 yr.	3 yrs.
Personal Rate	400	1000
Standard Rate	500	1200
Reduced Rate	250	x
Life Membership	**3000**	**10 Yrs**

Standard rate is for Institutions and Libraries
Reduced rate is for undergraduate students, interns and those under-going post graduate courses
Foreign

	1 yr.	3 yrs.
Gulf Countries	100 SR	275 SR
Rest of the World	$US 100	$US 200

JK=PRACTITIONER The International Journal of Current Medical Science & Practice

Name ______________________________

Address ______________________________

____

Institution/Hospital ______________________________

Please tick box

☐ Yes send me JK-Practitioner

☐ Personal ☐ Standard ☐ Reduced

☐ I enclose a cheque/bank draft payable to the editor, JK Practitioner at Srinagar. (SBI, JK Bank or Grindlays Bank)

Expiry date ______________________________

Signature ______________________________

Date ______________________________

**Please return this order form to Dr. G.M. Malik, P.O.Box 884 GPO
Srinagar 190 001 (Kashmir)**

ANAESTHESIA AT THE PRIMARY HEALTH CENTRE

Abdul Ahad M.D.; Javid Manzoor M.D.

India is a developing country and majority of our population lives in villages and small towns where primary health centres form the core of our health services. Medical infrastructure and resources for health care at these centres and small hospitals are generally limited for a variety of reasons and as such anaesthetic and other specialist services are subject to a constraint of resources for want of trained personnel, proper equipment and drugs. A good number of patients with varied health problems visit these centres daily and many may require surgical intervention. Anesthetic service is therefore, essential and may be required too often to undertake both emergency and routine as well as major and minor procedures. Due to the shortage of trained and qualified anaesthesiologist, a medical officer who has one or two years of experience in the speciality may be called upon to perform the duties of an anaesthetist. In these constrained situations, the needs of a small hospital are best served by the regular use of relatively few and simple techniques that can provide good and safe anaesthesia for virtually any clinical situation and such techniques should depend little on external supplies and technical assistance.

Difficulties:-

1. Lack of trained anaesthesia technicians at PHC's. Skilled help is very essential especially while dealing ill and complicated cases as caesarean sections etc.
2. Shortage of anaesthetic gases and newer inhalational agents. Even oxygen may be in limited supply.
3. Availability of anaesthetic drugs particularly induction agents and muscle relaxants is such that there is hardly any choice left for the anaesthetist to choose from while taking into consideration the clinical condition of the patient and his laboratory parameters.
4. Lack of life saving drugs, antibiotics and particularly I/V fluids may make dealing a complicated case difficult.
5. Equipment and gadgets like ECG monitor, pulse oximeter, NIBP, capnography which have become basic monitoring for present day anaesthesia, are lacking and the anaesthetist has to depend on parameters like pulse, blood pressure (sphygmomanometry), colour of the patient and peripheral perfusion.
6. Inadequate resuscitative facilities in term of:-
   a) Lack of resuscitative equipment e.g. cardiac defibrillator and resuscitative drugs.
   b) Lack of expert specialist help in cases of anaesthetic complications.
7. Un-availability of regular servicing facilities for the equipment and anaesthetic apparatus and other equipments.
8. Lack of good laboratory backup and transfusion facilities.
9. Here may or may not be a proper operating room or recovery area and may have to work in make-shift operating room subjecting the patient and the staff to hostile weather and environmental conditions.
10. These small hospitals may not have efficient transport system and lack trained shifting personnel.
11. Un-availability of proper sterilization system for the anaesthetic equipment.
12. There is usually no reservoir of common and essential drugs and no spare equipment at such centres.

Aims:

Inspite of all these difficulties and constraints, an anaesthetist can provide lot of services at such centres. He should make himself well versed with the environment and the facilities that are available to him. His aim should be to provide safe anaesthesia to his patients with the trusted techniques and equipment and not experiment too much. His aim should be:-

1. To select patients especially for cold surgery and try to predict expected problems if any e.g. difficult intubation etc.
2. Monitoring the patient closely per-operatively by use of simple parameters like pulse, blood pressure and colour of the patient.
3. To use regional anaesthetic techniques like spinal anaesthesia and nerve blocks whenever the situation permits.
4. Use of safer and commonly available anaesthetic agents like ether and ketamine.

Before embarking on any anaesthetic technique or procedure it is important that the anaesthetist assesses

JK-Practitioner 1999; 6(2): 164-167
From the Department of Anaesthesia, Govt Medical College Srinagar , India (Prof Ahad, Javid)
Received Febuary 1999 Accepted March 1999

Correspondence: Dr. Javid Manzoor, Registrar Anaesthesiology, SMHS Hospital, Govt Medical College Srinagar Kashmir J&K , India.

himself that he has some basic skills which are vital for the care of the critically ill and anaesthetized patients. These broadly include:-

1. He should be able to make assessment of the critically ill and/or unconscious patients in terms of:-
    a) Airway
    b) Breathing
    c) Circulation
    d) Brain
    e) Other Injuries
2. Care of the airway. He should be skilled to maintain a patent airway by:-
    a) Repositioning the head and neck.
    b) Clearing the mouth and oropharynx of secretions.
    c) Inserting an artificial oropharyngeal or nasopharyngeal airway.
    d) Endotracheal intubation.
3. He should be able to recognize and take care of the patient whose breathing is inadequate by:-
    a) Mouth to mouth or mouth to nose breathing with expired air.
    b) Ventilation with self inflating bag or bellows with or without intubation.
4. Management of circulation by securing of one or two good I/V lines as per the need and restoring the circulating volume by crystalloids and colloids and blood if available.
5. As the treatment is instituted, the anaesthetist should to able to assess the improvement or deterioration in the condition of patient and act accordingly.
6. Transportation of the critically ill. Patient may need to be removed to operation theatre or ward or another hospital for further treatment. Before any such move, the patients condition should be reasonably stable and all attempts should be made to shift the patient with all resuscitative equipment taking particular care of the airway and other injuries (e.g. spine injuries).
7. Anaesthetist at the peripheral hospital should be knowledgeable about the techniques of cardiopulmonary resuscitation.

Choosing and Planning an Anaesthetic Technique:-

Anaesthesia practitioner during this tenure at a peripheral hospital has to deal different types of surgical procedures viz. general surgical, obstetric and Gynae, ophthalmology, ENT and orthopaedics. These could be both short and long procedures. The anaesthetic technique of choice in any given situation depends on the training and experience, the range of the equipments and drugs available and the clinical situation. One golden rule is worth remembering.

"However strong the indication may seem for using a particular technique, especially in an emergency, the best anaesthetic technique will be one with which you are most experienced and confident."

Some of the factors to bear in mind when choosing the anaesthetic technique are:-

a) Training and experience of the anaesthist and surgeon.
b) Availability of drugs and equipment.
c) Medical condition of the patient.
d) Time available.
e) Emeregency or elective procedure.
f) Presence of a full stomach.
g) Patients's preference.

Suitable anaesthetic techniques for different types of furgery

Type of surgery	Suitable technique
1. Head and neck surgery Upper abdominal, Intrathoracic	1. General endotracheal anaesthesia (G.A)
2. Lower abdomen, groin, Perineum and lower limbs.	2. GA, Spinal anaesthesia, nerve or field block or combined general and conduction anaesthesia.
3. Upper limbs.	3. General endotracheal, I/V regional anaesthesia.

Commonly used anaesthetic techniques at a peripherial hospital are:-

1. General anaesthesia with drugs given intravenously or by inhalational method.
2. Conduction anaesthesia.
3. Light general anaesthesia can be combined with a regional technique to a greater advantage.

General Anaesthesia

The aims of general anesthesia are:

1. Pleasant induction.
2. Good operating conditions for the surgeon.
3. Lack of awareness.
4. Safety for the patient.

No single anaesthetic agent has all the qualities, therefore it is a common practice to combine several drugs, each of which provide a single component of anesthesia. This can be represented as a triangle whose corners represent sleep (unconsciousness), muscular relaxation and analgesia (lack of response to painful stimuli).

Anaesthesia is induced either by inhalational method using ether or halothane or by I/V induction agents like STP or ketamine. After endotracheal intubation patient can be maintained on one of the inhalational agents, breathing spontaneously or paralysed with a neuromuscular -blocker (NMB) and IPPV instituted, adding a lower concentration of halothane or ether. Anaesthetic apparatus used can be either continuous flow machines (like Boyles machine) or a draw-over system (like EMO, OMV).

Continuous flow machines require compressed gases for use and great care is needed to avoid the accidental delivery of hypoxic to the patient. These machines can be used only if there is a continous and granted supply of gases like N_2O and O_2. These gases are difficult to obtain at district and PHC level and also N_2O is very expensive. Exhaustion of oxygen supply may lead to delivery of N_2O only to the patient and this can be disastrous. Various alarms and interlocks have been fitted but none is fully satisfactory. Besides these machines are itself costly and may need repeated servicing and checks which may be difficult to achieve at such centres.

A draw-over system which is open to atmosphere at one end can not deliver substantially less than 21% of oxygen and can be used even if no oxygen can be done very easily. This system is capable of producing good anaesthesia and surgical condition. A good example of this sytem is the EMO (Epstein-MacIntosh-Oxford) vaporizer. It has proved extremely reliable easy to understand and maintain and economical in use. It should be the first choice for inhalational anaesthesia in a small hospital. The EMO vaporizer is 24 cm high, has diameter of 23 cm and weight of 6.5 kgs when the water compartment is full. It will deliver a predetermined concentration of either vapour in air. A water compartment of approximately 1200 ml acts as a heat buffer. It is usually employed as a draw-over apparatus but if combined with oxford inflating bellows, it can be used for IPPV. Ether and air can be used after thiopentone or inhalational induction.

The draw-over system can be also used for paediatric patients by replacing the adult size breathing valve with an infant size valve that has a smaller internal diameter and dead space. If possible replace the adult size side inflating bellows (SIB) with small bellows or infant resuscitator bag. Any child under 10 kg body weight should be intubated and ventilation controlled. Drawover system can be converted to a continuous flow mode, either with a farman entrainer or by connecting a flow of O_2 (or O_2 & N_2O) to the side arm of the oxygen enrichment T-piece and closing off the open end. Ayre's T-piece is used for children and either spontaneous or controlled ventilation can be employed.

The OMV (oxford miniature vaporizer) can be calibrated for halothane or trichloroethylene and also can be used with bellows. The recommended inhalational agents for draw-over apparatus is either (e.g. with EMO) halothane and trichloroethylene (With OMV). Ether is preferred at district hospital because of its distinct advantages over other agents. It is:-

a) Relatively non-toxic
b) Cheap and readily available
c) Provides excellent relaxation without severe respiratory depression.
d) Respiratory depression with overdosage is not accompanied by cardiac depression.
e) May be treated with IPPV.

Disadvantages include:-

a) Risk of explosion and fire with oxygen or N_2O
b) Has a peculair irritating smell.
c) Has slow induction and recovery.

Ketamine Anaesthesia:-

This technique is suitable when muscle relaxation is not required especially in children. It does not require any anaesthetic apparatus and is relatively safe.

Ketamine is a unique drug. In anaesthetic doses it produces a trance-like state of "dissociative anaesthesia" which consists of profound analgesia with only slightly impaired pharyngeal and laryngeal reflexes. There is a sympathetic activation with mild cardiovascular stimulation and smaller increase in heart rate and blood pressure. The induction dose is 1-2 mg per kg I/V and 6-8 mg/kg I/M. Anaesthesia can be prolonged by small incremental doses. Ketamine anaesthesia is suitable for shorter cases and orthopaedic manipulations especially in the young people and children.

For procedures requiring relaxation and also for more general use, ketamine can be given by infusion (1mg/min) in combination with muscle relaxants and IPPV with air.

Conduction Anaesthesia:-

In this the techniques include epidural anaesthesia, spinal anaesthesia, infiltration anaesthesia, field blocks, specific nerve blocks and intravenous regional analgesia.

1. **Epidural** techniques are more difficult, take longer, to perform and are less predictable in their effects and as such are not ideal for a peripheral hospital.
2. **Spinal** anaesthesia. In this condcution block of nerve roots is achieved by injecting a small volume of concentrated local anaesthetic solution into the subarachnoid space through a lombar puncture (L.P) needle. L.P is made between 3rd and 4th lumbar vertebrae in sitting or the lateral position. The local anaesthetic drugs used are lidocaine 5% (heavy) or bupivacaine 0.5% (heavy). All precautions to ensure proper sterlization of the needle and preparation of the dpart should be taken. If available disposible sets should be used.

   Successful spinal anaesthesia produces a considerable block of sympathetic nerves resulting in wide spread vasodilatation and fall in blood pressure which should be prevented by preloading the patient with 0.5 to 1 liter of crystalloid or colloid solution. Spinal anaesthesia can be used for almost any operation in the lower abdomen (e.g. caesarean section), perineum or lower limbs. It gives very good relaxation and the technique is simple and easy. Lidocaine provide an operating time of about 90 minutes while as bupivacaine can last for 2-3 hours. The main contraindications to this type of anaesthesia include:-

1. A hypovolemic, dehydrated or shocked patient.
2. Uncorrected anaemia or heart disease.
3. Patient on anticoagulant therapy.
4. Local sepsis.
5. Severe spinal deformities.

3. **Simple Infiltration:-** This consists of infiltrating the skin by a dilute local anaesthetic solution, for example lidocaine 0.375-1% and bupivacaine 0.125%. This duration can be increased by addition of adrenaline (1,200,000) while using lidocaine.
4. **Field Blocks:** The principle of field block is to lay down a barrage of dilute local anaesthetic drug to block all the sensory nerves supplying a particular area. It is used for areas where nerve supply is complex and variable e.g. for repair of inguinal hernia and for caesarean section. Lidocaine 1% with adrenaline is generally used.
5. **Nerve Block Techniques:** The aim here is to deposit local anaesthetic next to a specified nerve to block sensation from the area that it innervates. Lidocaine 1-2% is used for this purpose. These nerve blocks are learned by experience and are very helful for surgery on the limbs. Examples of nerve blocks are:-

   Digital nerval block, nerve block at the ankle, axillary block of the brachial plexus, block of inferior alveolar nerve (dental block), intercostal nerve block, femoral nerve block etc.
6. **Intravenous Regional Anaesthesia:-** This technique consists of I/V injection of local anaesthetic drug into an arm that is isolated from the circulation by an arterial tourniquet. There is risk of absorption of local anaesthetic drug into the circulation after release of tourniquet. So resuscitative facilities should always bo available.

Suggestions:

An anaesthetist can be an asset at a peripheral hospital and every effort should be made by the concerned authorities that his job and working conditions are made better and favourable for the patients and for the hospital.

Few suggestions are made in this regard:-

1. Regular and improved hospital supplies of anaesthetic gases and all essential and common drugs.
2. Providing of basic monitoring devices and resuscitation facilities.
3. Regularly recruiting and training courses of anaesthesia technicians and staff.
4. Refresher courses for anaesthetists to update their knowledge about the subject.
5. Regular servicing facilities for anaesthesia machines and other equipment.
6. Arranging C.P.R. courses for hospital staff and nurses in general and anaesthesia personnel in particular.
7. Anaesthesia training should include teaching of draw-over system in teaching hospitals and their intermittent use and demonstration to trainees.

Anaesthesia is now much safer than it was 50 years ago. Improving the basic facilities and training at these small hospitals will benefit the poor rural people in general and also reduce the load on the central hospitals.

MEASLES, MUMPS, RUBELLA (MMR) VACCINE-NEW STRATEGIES

Mohd Farooq Mir M.D.; Amarjeet Singh Sethi M.D.; Mohd Mubarik M.D.

Introduction:

Measles, Mumps and Rubella (MMR) three vaccine preventable diseases are as old as man itself. MMR is a live attenuated triple vaccine (Viral). Vaccine has been available now for a long period of time. However, its extensive use has been made recently, when it was observed that two or more than two viral vaccines do not interfere with each other and widespread outbreaks of measles and rubella were reported in older children.

Measles:

It has been in particular a leading killer disease with mortality resulting from bronchopneumonia and meningoencephalitis. High morbidity has been associated with measles, particularly in undernourished children of developing countries. By anergy it flares up latent tuberculosis. Children at brink of malnutrition become frankly malnourished (Kwashiorkor). Before the advent of measles vaccines (Schwarz, Edmondston B and now Endors Edmondston Strain)in 1968, the disease was epidemic and swept all continents of the world (U.S.A> alone had 400,000 cases per year), though it has been reduced to sporadic form now. Contrary to previous belief the disease erupts in immunized children also, though in mild form if primary vaccination has been done in Ist year of life. This emphasizes need for MMR as booster for measles.

Mumps:

A benign disease in children is making its reappearance in school and college going children with its potential complication of subfertility (males) from epididymo-orchitis to diabetes mellitus in nonfatal pancreatitis Mumps embryopathy has been linked with definite fetal wastage and probable hydrocephalus (aqueductal stenosis) and endocardial fibroelastosis. Despite live attenuated vaccine (Jeryl Lynn Strain) available for more than two decades, routine vaccination to prevent this disease has not been taken up particularly with our set up.

Rubella:

(German measles) though an inapparent illness in children, assumes devastating form when it strikes pregnant women. The whole spectrum of probable fetal involvement to full blown congenital rubella syndrome with ophthalmic (Cataract, Microphthalmia, Glaucoma, Retinopathy) auditory (Sensorineural deafness), cardiovascular (PDA, VSD, ASD) and neurological (Growth retardaton, Cerebral palsy) involvement is alarming. Disease has been on decline since vaccine was licensed in 1969. (RA 270/3 diploid cell culture as Rubella vaccination programme) However, desired attention has not been focussed on its preventable aspects.

Role of MMR:

Two viral vaccines interfering with each other's immune response (interference Phenomena) is no longer held valid, hence the role of triple antigen (MMR) is no longer disputed.

Apart from serving as measles booster for those who had measles vaccination at 9-10 months of age, it prevents Rubella and mumps in children and women of bearing child age. This has led advisory committee on Immunization practice (U.S.A.) to publish revised recommendations in 1998 as under:-

1. A dose of MMR be given at 12-15 months age and repeated at 5-6 years of age.
2. Two doses of MMR for school entry, so that all school going children be vaccinated by two doses of MMR by year 2001.
3. All people working in health care facilities should have acceptable evidenceof measles and Rubella immunity.

However in our set up, where measles erupts as early as 6 months of age and maternal antibodies are not significant beyond 6 months of age, these recommendations have been modified by IAP (Indian Academy of Paediatrics) as under:-

1. Measles be given at 6 months of age followed by MMR at 15-18 months or,

JK-Practitioner 1999; 6(2): 168-169
From the Department of Pediatrics Govt. Medical College Srinagar India, (Mir, Sethi, Mubarik)
Received Febuary 1999 Accepted March 1999

Correspondence: Prof. A.S.Sethi, HOD of Pediatrics Govt. Hospital for Children Srinagar

2. Ist dose of MMR be given at 6 months of age and repeat dose at 3-5 years of age.

MMR:

A polyvalent Lyophilized live attenuated vaccine.

Composition:-

1. Enders Edomondston Strain (measles)
2. Jeryl Lynn Strain (Mumps)
3. R A 270/3 diploid cell (Rubella)

Dose:

0.5 ml Subcutaneously,

Schedule:

Ist dose at 12-15 months
2nd dose at 3-5 years.
Individuals not responding to measles component of Ist dose of MMR responsed to 2nd dose.

Side Effects:

Common:

1. Local Pain
2. Induration
3. Edema.

Rare:

1. Anaphylaxis especially in those with history of allergy.
2. Fever, rash and lymphadenopathy especially with measles component.
3. Thrombocytopenia especialy in patient with ITP & thrombacytopenia of other causes.
4. Arthralgias, arthritis, arthropathy (Rubella Component).
5. Aseptic meningitis (Mumps component), now rare with Jerly Lynn strain.
6. Febrile seizures (incidence of 1:3000).

Precautions and Contraindications:

1. Pregnant women
2. Women of child bearing age to be counselled against conceiving within three months of vaccination.
3. People with egg allergy
4. Thrombocytopenia
5. Immune deficiency states.
6. In H.I.V. cases response variable, though no higher risk of complications.

References:

1. Kenneth J. Bart: Immunization practices. In Nelson's text book paediatrics 11996; I-WB Saunders, 15th edition; 106-18.
2. Morbidity and mortality weekly report U.S Deptt. of Health and Human service. May 22, 1998; Vol 47; No. RR8.
3. Penelope H., Dennehy; Georges Peter: New developments in childhood immunizations. Paediatric infectious diseases. Panthers publishers 1997; 92.

CHECKLIST FOR SUBMISSION OF MANUSCRIPT

— Covering letter including copy-right release

— Three copies of manuscript on A-4 size paper

— Name and address of author responsible for correspondence about the manuscript, including highest degree and affiliations of each author.

— Abstract (upto 150 words) along with 3-6 key words

— Running title (5-6 words)

— Three glossy prints for each illustration (10 cm × 8 cm), appropriately labelled and each illustration is cited in the text. Submit the legends on a separate sheet in the manuscript.

— Check all references for accuracy and completeness. Put references in proper format in numerical order, making sure each is cited in the text.

A HISTORY OF DIALYSIS

Ancient to classical period

The first recorded method for cleansing the blood was bloodletting. Papyrus writings mention that bloodletting or venesection was common practice in ancient Egypt. Lancets and cups used for this purpose have been found in burial vaults. Cups were usually cattle horns with holes drilled in the pointed ends through which the blood was drawn out by suction.

Hippocrates (c. 460-377 B.C.), who popularized bloodletting in the classical period, wrote that "venesection holds the first place in conducting the treatment..."[1] of a long list of diseases ranging from epilepsy and apoplexy to peripneumonia and "pleuritic affections." The operation was usually performed on the arm, but also on other parts of the body related to the inflamed or painful organ. Considerable quantities of blood were removed for therapy, sometimes until the patient fainted.

The influence of Greek medicine prevailed in ancient Rome. Celsus (53 B.C.07 A.D.) regarded bloodletting as the chief way to extract toxic waste from the body, observing that it was used as a remedy in almost every disease. He tied vessels during continuous bleeding, carrying out Hippocrates' recommendation that the vein be opened on the same side as the lesion, but intimated that opening a vein on the opposite side was already coming into medical vogue.

Aulus Cornelius Galen (200-300 A.D.) sometimes opened an artery. He was the first to advocate that specific quantities of blood be removed, preferably from 7 to 24 ounces at a time.

Another means of removing wastes from the body is through the skin, the largest organ of the body. It is recorded that the Minoans, ancient Egyptians, and Summerians all built baths for ceremonial cleansing and for curative purposes. In 500 B.C. the Scythians built the first steam bath, a felt tent hung over a tripod. Water and hempseed were thrown over red-hot stones to produce the vapour. But the Greeks were the first to use bathhouses for relaxation and restoration of general well-being, as well as for lectures by philosophers, men of science, and poets, and for athletes' games.

Roman soliders carried their taste for Greek pleasure baths back home; at one time, there were almost 900 public baths in Rome. Nothing was too elaborate or expensive for the baths, which became social and cultural centers forthe Romans. The baths were constructed of the most beautiful marbles of the world, and outfitted with paintings, sculpture, precious metals, and gems. The Baths of Caracalla had a 115-foot-diameter domed circular room, or Caldarium, for steam baths, and could accommodate 2000 bathers.

The origins of dialysis are thus found in ancient times when man first attempted to rid the body of impurities through vapour baths and to prevent or cure disease through venesection.

Middle Ages

The Roman Baths, known for their grandeur and elaborate design, were part of the heritage of the Middle Ages. As the Roman empire grew, so did public demand for more and more luxurious baths. Bathhouses had gardens, a stadium, shops, and open courtyards for poetry readings or lectures. The most magnificent baths were the Baths of Diocletian, built in Rome in 298-305 A.D. They could accommodate 3,200 bathers and were used extensively for relaxation and pleasure.

But hundreds of years later the grand Greek and Roman baths disappeared and were replaced by the homely, single-person wooden tub of the Middle Ages.

In the Middle Ages, a new dominant figure appeared to practice "medicine" —the barber surgeon. The barber was often a bathkeeper too, performing bleeding and cupping in the bathhouse.

During this period, the Greek and Roman philosophy of bloodletting prevailed and was practiced in Byzantium, or Istanbul. A well-known. Byzantine surgeon, Antyllus, sometimes opened the occipital, auricular, frontal, and temporal arteries. Followers of Galen, the renowned Greek physician, required, however, that venesection be derivative, or on the opposite side of the lesion.

In Italy, bloodletting became so popular that on Sundays, country folk would visit nearby villages and towns to be relieved of all "superfluous" blood. In addition, strong purges were given. Although physicians still continued to order venesection, they shunned its practice and the barber was allowed to monopolize

JK-Practitioner 1999; 6(2): 170-172

From Dr. GR. Nahami, Sheffield, South Yorkshire (u.k.)

bloodletting. Examinations for a medical license were not required, and barbers, carpenters, and blacksmiths frequently gave up their trades to perform bloodletting. Bloodletting was also performed by monks who followed the common practice of the period when everybody firmly believed in its efficacy.

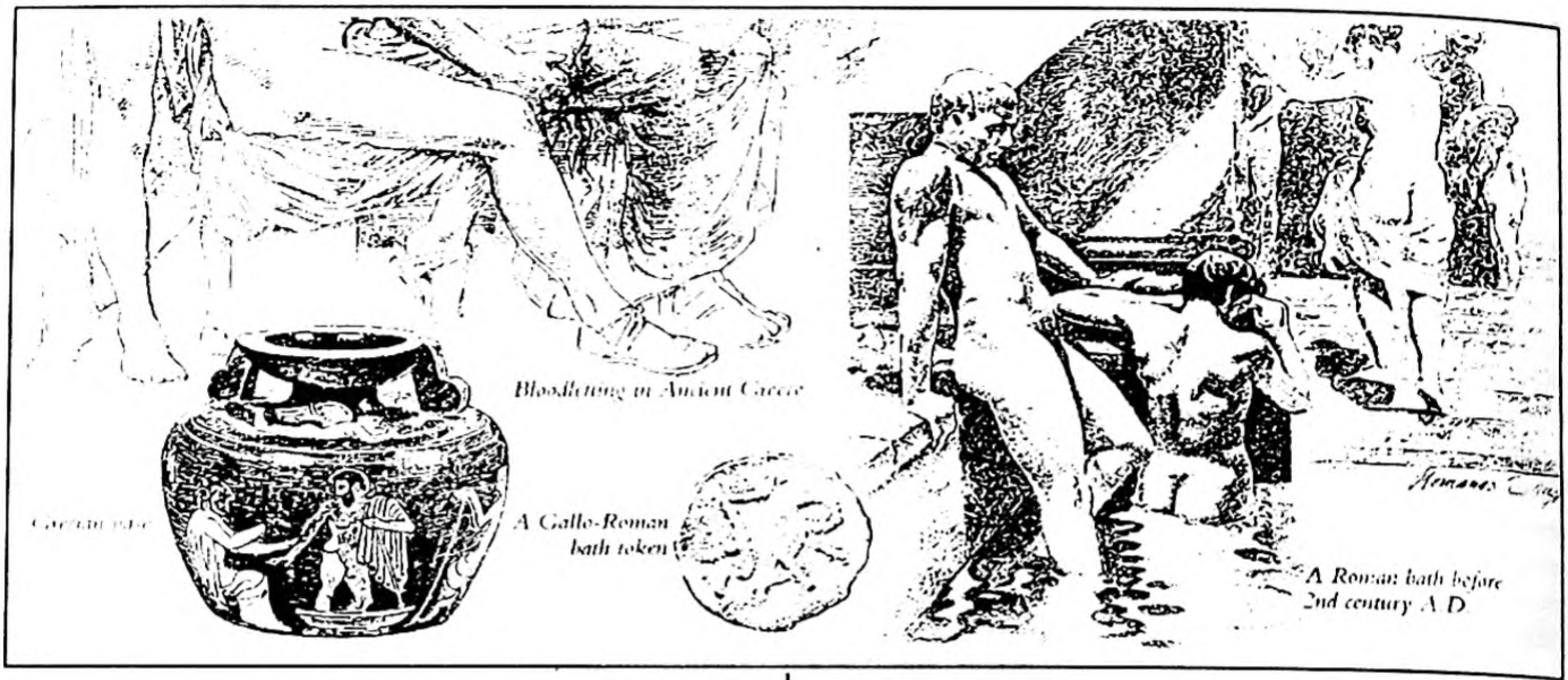
Gradually, surgery, which was considered degrading by physicians, was separated from medical practice. In fact, surgery was removed from the curriculum of mediaeval universities. So venesection went to where it was welcome-to the barbers, bathkeepers, and strolling "incisors," who were as likely to kill as to cure.

From the harmless and possibly curative use of the Roman baths to encourage blood cleansing through the skin, evolved the practice of bloodletting in the Middle Ages. Despite its overuse and controversy, however, bloodletting provided a necessary path toward the understanding and practice of dialysis today.

The Renaissance

The Renaissance, the period of great cultural and intellectual advancement that spanned the 14th through the 16th centuries, was a time of sharp contrasts. Highly accurate anatomical drawings by Vesalius and daVinci and the literary excellence associated with Elizabethan times existed side by side with such ancient practices as bloodletting. The Renaissance was also the age of the common public bath, which had the supposed healthful purpose of cleansing the body through the skin.[2]

But by the 15th century, public baths had become notorious for promiscuous bathing and were condemned by the monks as hotbeds of vice. Prints of the period show men and women in a large tub or steaming bathroom eating, drinking, reading or playing muscial instruments. In the midst of this revelry, there usually was one patron undergoing venesection or bloodletting at the hands of the bathkeeper, who also served as barber-surgeon and bloodletter.



Bloodletting in Ancient Greece

Grecian vase

A Gallo-Roman bath token

A Roman bath before 2nd century A.D.

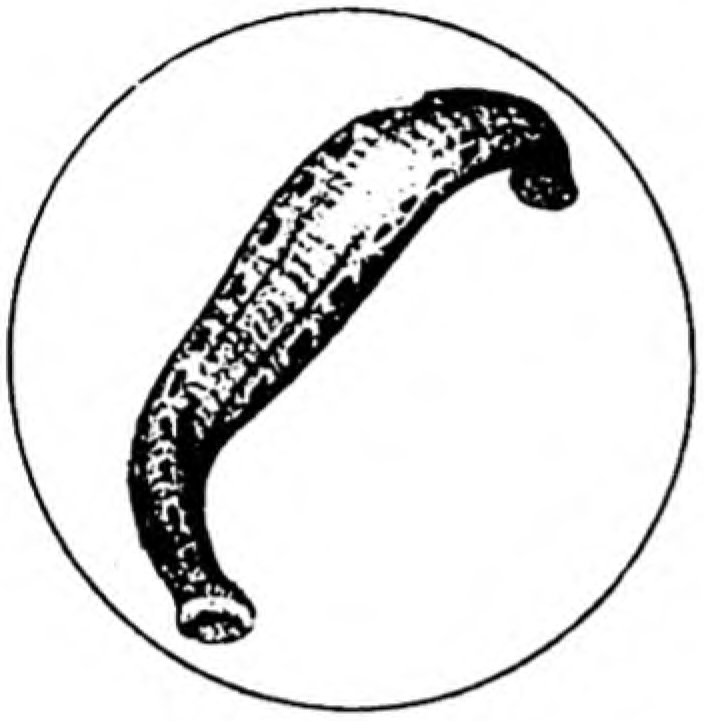
During the Renaissance, bloodletting was intimately associated with astrology, which was in vogue at most European courts. The medicina astrologica has unrestricted authority from the 13th to the 17th centuries and greatly influenced bloodletting. Because phlebotopmy was highly acclaimed as an essential remedy, a regimen for its use was divised based on star maps. Every vein known in the body was said to correspond to a star or planet, just as various body organs corresponded to signs of the zodiac. Following the popular belief that the life of each organ was controlled by the constellations, phlebotomists believed they could diagnose the cause of all ailments by reading the position of the stars.

Venesection manikins, or "zodiac men," were constructed to aid in treating illness, with ailments and venesection points shown on the manikin. There were 53 venesection locations that could be bled, with each point related to four, five or more disorders. Thus, the number of potential bloodlettings could reach the hundreds.[3]

Bloodletting was not always preceded by a medical examination and venesection was practiced even in the absence of illness. During this period, however, there were physicians who not only rejecterd the tenets of the medicina astrologica, but highly disapproved of venesection and its insane waste of blood. But the voices of moderation went virtually unheeded, and volumes of blood continued to be drained from patients. Despite its unscientific beginnings and association with the occult, the practice of bloodletting proved to be part of a long process that led to the development of modern dialysis.

Nineteenth and Early Twentieth Centuries

Medical knowledge advanced rapidly during the 19th and 20th centuries. Practices such as bloodletthing that had been in existence for centuries gradually gave way to newer procedures. Physicians recognized the need to purify the blood without draining it and hence, modern hemodialysis slowly evolved with modifications through the years.



In the wake of the Industrial Revolution, physicians were increasingly questioning the use of venesection. One such French physician, P.C. Louis, kept records of his patients in the 1820s. He concluded ".......bloodletting has had very little influence on the progress of pneumonitis, of erysipelas of the face, and of angina tonsillaris....we do not.....arrest inflammations[4]."

However, well into the 19th century, bloodletting still had its advocates. Dr. Heinrich Stern practiced venepuncture, "the direct insertion of a needle or a trocar into a vein for the sake of withdrawing blood or for the intravenous introduction of saline solution...."[3] Leeching was also popular, and in one year, 40 million leeches were imported into France.

Another aspect of bodily cleansing, the public baths, continued to be an integral part of community life and flourished with the development of plumbing in England. They were meant to cater strictly to health and physical welfare and came to be replaced in time by private baths.

With the advent of sulphuric ether and chloroform in the 19th century, bloodletting was no longer used for anesthetic purposes. Venesection was further discredited with the use of homeopathy and the Priessnitz system of hydrotherapy for treatment of inflammatory diseases.

Scientists were beginning to realize that only certain elements in the blood were harmful and needed to be removed. In 1913, Abel, Rowntree, and Turner postulated the use of external dialysis of blood. The apparatus they designed circulated an animal's blood through collodion tubes surrounded by a rinsing solution of 0.6% sodium chloride. The group extracted salicylate from the blood of two dogs that approximated amounts removed by normal kidneys[5].

In the following decades, investigators experimented with dialysis so that numerous difficulties were overcome and vast improvements made.

References:

1. Hippocrates: Genuine Works, Adams F (trans). New York, 1886; 1:261.
2. Wilson WJE: The Eastern or Turkish Bath with its History, Revival in Britain and Application to the Purposes of Health. New York, Miller, Wood & Co. 1866, p 36.
3. Stern H: Theory and Practice of Bloodletting. New York, Rebman Co., 1915, p 26-29.
4. Louis PC: Effects of Bloodletting in Some Inflammatory Disease and on the Influence of Tartarized Antimony and Vesication in Pneumonitis, Putnam CG (trans). Boston, Hilliard Gray & Co., 1836, p 22.
5. Doyle JE: Extracorporeal Hemodialysis Therapy in Blood Chemistry Disorders. Springfield, Illinois C Thomas Publishers, 1962, p 10-13.

MEDICINE UPDATE - 1998

Fayaz A. Bhat M.D.

HIV infection

Randomized controlled trials using 2 nucleoside analogues plus a protease inhibitor[1,2] showed remarkable efficacy in increasing T-cell counts, reducing viral load, slowing the rate of progression to AIDS, and improving survival in patients with fairly advanced HIV infection. These trials provide strong support for the use of a 3-drug regimen for patients with significant viral activity. However, basic science research[3,4] showed that even patients with suppression of viral load below the detection limit for up to 2.5 years have recoverable virus in peripheral blood monouclear cells, although no evidence of drug resistance existed. Therapy for HIV infection is complicated and expensive but can provide dramatic clinical benefit, at least in study situations. Compliance with these complicated regimens is critically important for their continued benefit.

HIV-1 RNA levels continue to predict outcomes better than CD4+ counts, and the combination can predict progression to AIDS and death[5]. Using viral load to monitor response to therapy improves care and is recommended in published treatment guidelines[6,7]. Prophylaxis of tuberculosis in anergic patients with HIV infection was shown to be of no significant benfit[8]. Finally, 1 study showed a community-based prevention program to be quite successful by self-report in limiting risky behaviors[9].

Hormone replacement therapy

This year's update includes 2 studies that support the benefits of HRT[10,11]. A 15-year, case-control study of women in the Nurses' Health Study[10] showed that current hormone users had a lower relative risk for death (0.63) than did women who had never used hormones. Benefits of HRT were greatest in patients with coronary risk factors and out-weighed the increase in mortality from breast cancer. Furthermore, women with a first-degree relative who had breast cancer did not have a significant increase in their risk for breast cancer during the study period.

Osteoprosis

Sudies published this year provide guidance about preventing osteoporosis in health older patients[12], women with existing fractures[13], and patients at increased risk because of underlying diseases[14]. A randomized trial of healthy ambulatory men and women older than 65 years of age showed that calcium (500mg) plus vitamin D (700 IU) prevented bone loss and decreased the incidence of non-vertebral fractures[12]. For postmenopausal women with evidence of osteoporosis (low bone-mineral density and evidence of at least 1 vertebral fracture), a randomized trial[13] found that alendronate (5 mg) decreased the frequency of radiographic and clinical fractures compared with placebo for a period of 3 years. The number needed to treat (NNT) to prevent clinically apparent vertebral fractures for 3 years was 37. Women at risk for developing osteoporosis because of corticosteroid therapy may also benefit from use of etidronate therapy[14].

Cancer

Several studies on screening and early detection of prostate and colon cancer were published during the past year. For prostate-specific antigen (PSA) screening Catalona and colleagues [15] found a 22% prevalence of prostate cancer in asymptomatic mean with PSA levels of 2.6 to 4.0 prevalence of prostate cancer in asymptomatic men with PSA levels of 2.6 to 4.0 ng/mL. 83% of the cases were clinically significant by histopatologic criteria.

Rectal bleeding is disconcerting to patients, and new data reaffirm its importance. Helfand and colleagues[20] studied patients with rectal bleeding noted on review of systems. 23% of patients had a serious cause of bleeding including 6.5% who had colon cancer and a third of these cases were poximal. Read and coworkers[21] reported that the incidence of proximal neoplasia was significant in patients with small adenomatous polyps (≤ 5mm) discovered at the time of screening sigmoidoscopy. 29% of such patients had a proximal neoplasm, which was advanced in 6% of patients. Patients with rectal bleeding or small distal polyps warrant a full evaluation of the colon.

Cardiovascular disease

Important advances were published on coronary artery disease (CAD), hypertension, stroke, and venous thromboembolism. Patients having noncardiac

JK-Practitioner 1999; 6(2): 173-174
This Medicine update was prepared by Reviewing the 1998 articles regarding the problems we see in our General Medical Practices.
From Fayaz A. Bhat MD, Dept.. of Medicine SKIMS Soura, Srinagar.

procedures randomized to atenolol compared with placebo had a 60% relative risk reduction and a 12% absolute risk reduction in 2-year mortality[12]. Treatment was started before surgery and stopped at discharge.

The Systolic Hypertension in the Elderly Program (SHEP), which studied diuretic-based, stepped care approach of isolated systolic hypertension, showed a protective effect in preventing congestive heart failure[26]. The relative risk for fatal and nonfatal heart failure was 0.51 in patients receiving diuretics compared with placebo (NNT=48) after 4.5 years of follow-up. Benefits were particularly pronounced in patients with a history of myocardial infarction.

For stroke care, an important randomized trial compared the use of aspirin and heparin in patients presenting with acute ischemic stroke[27] and found that the use of aspirin for 14 days led to fewer recurrent strokes and a reduction in the rate of death or dependency at 6 months' follow-up. Heparin did not show similar benefits. A major meta-analysis[28] reported that lowering cholesterol with HMGcoA reductase inhibitors reduced the overall risk for stroke and total mortality in patients with known CAD.

Venous thromboembolism was the topic of 3 important studies. A randomized trial showed that patients with a second episode of deep venous thrombosis (DVT) or pulmonary embolism (PD) should receive anticoagulation therapy indenfinitely to prevent further recurrences. In addition, 2 randoomized trials showed that low-molecular-weight heparin has not been shown to be superior to unfractionated heparin, but it seems to be a suitable alternative to standard therapy with unfractionated heparin for DVT and PE[29].

D-dimer levels may be useful to rule out PE in outpatients. A prospective study[32] of emergency department patients found a sensitivity of 99%, specificity of 41%, negative predictive value of 99%, and negative likelihood ratio of 0.02 for a D-dimer level <500 ug/L. If these results are confirmed, D-Dimer levels <500 ug/L would virtually rule out the diagnosis of PE.

Asthma

2 randomized trials provided useful approaches to asthma control. Lowdose theophylline plus low-dose inhaled steroids seemed to be as effective as higher doses of inhaled steroids in preventing the symptoms of moderate asthma. In addition, the use of inhaled long-acting ß-agonists provided added benefit to inhaled glucocorticoids in preventing asthma symptoms and severe and moderate exacerbations[29]

References:

1. Gulick RM, Mellors JW, Havlir D, et al. N. Engl J Med. 1997; 337: 734-9.
2. Hammer SM, Squires KE, Hughes MD, et al. N Engl J Med. 1997; 337: 724-33.
3. Wong JK, Nezareh M, Gunthard HF, et al. Science. 1997; 278: 1291-5.
4. Finzi D, Hermankova M, Pierson T, et al. Science. 1997; 278: 1295-300.
5. Mellors JW, Munoz A, Giorgi JV, et al. Ann Intern Med. 1997; 126: 946-54.
6. Hughes MD, Johnson VA, Hirsch MS, et al. Ann Intern Med. 1997; 126: 929-38.
7. Carpenter CC, Fischl MH, Hammer SM,, et al. JAMA. 1997; 277: 1962-9.
8. Gordin FM, Matts JP, Miller C, et al. N Engl M Med. 1997; 337: 315-20.
9. Kelly JA, Murphy DA, Sikkema KJ, et al. Lancet. 1997; 350: 1500-5.
10. Grodstein F, Stampfer MJ, Colditz GA, et al. N Engl MEd. 1997; 336: 1769-75.
11. Sellers TA, Mink PJ, Cerhan JR, et al. Ann Intern Med. 1997; 127: 973-80.
12. Dawson -Hughes B, Harris SSk, Krall EA, Dallah GE. N Engl J Med. 11997; 337: 670-6.
13. Black DM, Cummings SR, Karpf BD, Et al Lancet. 1996; 348: 1535-41.
14. Adachi J, Bensen WG, Brown J, et al. N Engl J Med. 1997; 337: 382-7.
15. Catalona WJ, Smith DS, Ornstein DK. JAMA. 1997; 277: 1452-5.
16. International Stroke Trial Collaborative Group. Lancet. 1997; 349: 1569-81.
17. Hebert PR, Gaziano JM, Chan KS, Hennekens CH, et al. JAMA. 19971 278: 313-21.
18. Pauwels RA, Lofdahl CG, Postma DS, et al. N Engl MEd. 1997; 337: 1405-11.
19. International Stroke Trial Collaborative Group-Lancet. 1997; 349: 1569-81.
20. Hebert PR, Gaziano JM, Chan KS. Hennekens CH, et al. JAMA. 1997; 278: 313-21.
21. Levinson W, Altkorn D, Stern S, and Roach K. ACP Journal Club Aug 1998 A (12-14).

Name	:	***Muhammad Yahya Alvi***
Born	:	1936 in Kashmir
Schooling	:	Islamic School .
Academic Qualification	:	MBBS, MRCP, FACP.
Address	:	International Islamic University Malaysia University, 46700, Petaling JayaSetanger Darul Ehsan.
Present Posting	:	Medical Consultant Cum-Director Health Services/Malaysia.

- Completed MBBS from Madras in 1957 at the age 21 years.
- From 1957 - 60 worked in hospitals in Kashmir.In 1960 was offered the DIPLOMATIC assignment of VICE Counsel cum Chief Medical Officer in Indian.Embassy Makkah, Saudi Arabia where he worked for 5 years till 1965.
- In 1965 went to UK to pursue his studies in medicine and stayed there for a decade, working in different Hospitals - and was given honorary appointment of "Police Surgeon" - the first non-British to get that post.
- Obtained MRCP UK during this period and in years rose to be a Junior Consultant in different hospitals. Returned to Kashmir to take up honorary consultancy in Polyclinic of Sher-i-Kashmir Institute at Soura and also to do social and Dawah woirk, in addition to General Practice.
- Started and established an educational institute intergrating religious and modern education called Iqbal Memorial Trust of which he was the founder chairman. Also established a social service centre of which he was the Honorary President, for poor women and orphans - where handicraft was taught and work provided to give dignity and self-respect to the poor. This has since grown and now provides jobs to over 400 people.
- In the 80's he went to Alfatah University, Libya to teach Medicine at Tripoli.
- Left Kashmir in 1990 at the invitation of International Islamic University Malaysia and joined there as a Medical Advisor to commence a Medical Faculty there. Responsible for drawing up Medical Curriculum and planning the Medical College which is now fully operational. In 1993 appointed as Medical Advisor cum Director Health Services of the International Islamic University and established four modern Polyclinics run by international doctors tocater to the needs of our 20,000 population of students, staff and their dependants.
- Did Islamic Studies at International Islamic University in Malaysia and was awarded Diploma in Islamic Studies by the IIUM in 1993 after writing his thesis on "Modern Biomedical Issues - Islamic Prospective.
- Currently working as Director, Health Services cum Medical Consultant at the International Islamic University Malaysia.
- In 1995, in recognition of his services, he was awarded the membership of Malaysian Academy of Medicine, Malaysia a highly honoured body of Medical Specialist.
- In 1997, he was honoured by the Royal College of Physicians of London and was taken as a fellow and awarded FRCP London. Father of 5 happily married daughters-three doctors and two Islamic scholars and grandfather of 10 children, involved in active service at the age of 62.

Name : ***Mahmooda Khan***

Address : "*Shadman*" Rawalpora Sgr.

Date of Birth : 23-12-1934

Place of Birth : Srinagar.

Academic Qualifications: FRCS

- MBBS (1956) from Lady Harding Medical College N. Delhi.
- Speciality training in Surgery at Temple University Philadelphia (USA) FRCS London & Edinburgh (UK) till 1967.
- After graduation from Lady Harding Medical College New Delhi did House Job/Registrarship in Surgery from the same college till 1960 and for specialists training outside the country to return in 1969 to join at Govt. Medical College Srinagar as Associate Professor : 1969
- Professor 1974,
- Head of the Department of Surgery (1982 till retirement in the year 1993).
- Has written many Articles published in National/ International Journals and arranged many conferences.

Questions and Answers

Q.1. Why did you choose Surgery & not Gynecology?

Ans. I was always interested in being a Surgeon and I am glad that I have taken Surgery as a Speciality, inspite of the fact that I was the best outgoing student in Gynecology / obstetrics. It surprised a lot of people in its time including my father Dr. Col. G.A. Khan & my HOD of Gynecology. In short I was destined to be a surgeon-A female amongst a male dominated fraternity!

Q.2. Which Subspecialty of Surgery have you enjoyed most?

Ans. All subspecialities of Surgery are interesting and rewarding, but I was always fascinated by Paediatric, Plastic, Endrocrine & Vascular surgeries. The more challenging a job made it more enjoyable!

Q.3. Which speciality you suggest our female doctors to practice?

Ans. Female doctors should not be labelled as gynecologist only. A person should choose a profession which interests him/her most. It is a very individual selection. I can only comment that if a female doctor wishes to choose surgery, they should remember that it requires total dedication & lot of sacrifice to become a recognised surgeon, no matter what subspecialty one chooses.

Q.4. Don't you think to be a general Surgeon hampers with family life of female doctor?

Ans. I would like to question this question -why & how? I feel all professions require certain amount of time away from family and involves some compromise at family level. I have been lucky that I have had a supportive family who appreciated my efforts which I was putting in for my job. Without their support my job would have been/much more difficult.

Q.5. What suggestions do you give to your specialists in the field of Surgery?

Ans. My sincere advise to all surgeons is, that they should know when to operate & when not to operate. Keep away from knife if you can! Unindicated Surgery calls for trouble. Deal with the tissues with respect, it is a part of human body. And remember that the patient has trusted you with a knife, so try to do a work of art every time you operate.

Q.6. A word about Senior Surgeons you liked to work with?

Ans. I have had a lot of professional colleagues. As a trainee in Surgery, I admired most of my teachers. And as a teacher, I have taken pleasure in training my students, some of whom have become capable recognised surgeons. What I am today is due to the encouragement, which I have received by my teachers/colleagues during my training period in Philadelphia USA.

Q.7. What is the future of subspecialty in Surgery Viz-a-Viz General Surgery?

Ans. We would be entering year 2000 after one year. Technology has revolutionized Medical Sciences. We would soon see Robotics, Teleconferences in helping us in improving patient care. When technology knocks on our doors, we should implement it to improve upon our patient care. The surgeon should follow subspecialities, & do procedures what he/ she is competent in.

Q.8. Do you think it is an advantage or disadvantage if a couple belongs to Medical Profession and how?

Ans. In my view its a more compatible equation for couples to be of the same profession. This is true especially amongst Doctors. "It takes a literate person to read a book"- Thus for your spouse to appreciate your commitment and sacrifice, it would be necessary for him/her to have experienced the same.

Q.9. A word about private sector in Medical Education?

Ans. Its a need of time for the private sector to enter into this sector. But what should be stressed on is quality education rather than quantity. There should be a regulation to avoid mushrooming of Medical Colleges.

An additional word regarding Health Care System. We should prevent the emigration of young doctors way from home to improve health care here. This can be done by certain measures like increasing pay benefits, promotion prospects, higher speciality education etc. to doctors wishing to serve in the state.

Q.10. A word about JK Practitioner?

Ans. Its a commendable effort by Dr. G.M. Malik to have laid a foundation of a journal, to have its origin in Kashmir. It has good articles, with local, national & international contributions. I praise all the people who have put in an extra effort to create this journal.

INTERNATIONAL CONFERENCE ON RECENT ADVANCES IN MEDICINE - AN UPDATE

at
Sher-i-Kashmir International Convention Complex
(Centuer Hotel), Srinagar, Kashmir on August 21-22, 1999
For details contact:
i. Prof F A Khan, Chairman Deptt. of Medicine
Nassu County Medical Centre, East Meadow, New York 1155y.

ii. Prof G. M. Malik P.O. Box: 884, GPO, Srinagar, 190 001, Kashmir, India

2 **The First World Congress of Controversies in Obstetrics, Gynecology and Infertility, Geneva, Switaerland 29 July-1 August 1999**
Information: The First Congress of Controversies in Obstetrisc, Gynecology and Infertility, P. O. Box 50006 Tel Aviv 61500, Isreal

3. **Ninth National Conference of the Indian Association of Surgical Gastroenterology, Pondicheery, India 17-19 September 1999.**
Information: Prof. N. Ananthakrishnan, Department of Surgery, JIPMER, Pondicherry.

4. **Twenty Sixth International Congress on Occupational Health, Singapore 27 August - 1 September 2000.**
Information: Secretarial ICOH2000 c/o Department of Community, Occupational and Family Medicine, MD3, Lower Kent Ridge Road, Singapore 119260.

5. **International Congress on Atherosclerosis, Hypertension and Coronary Arteny Disease and Annual Conference of Indian Society of Hypertension at New Delhi**
For further details and registrations contact: Dr. H. S Rissam Organising Secretary, Escorts Heart Institute and Research Centre, Okhla Road, New Delhi-110025 India Fax: 91-11-6825013.

6. **World Stroke Congress, Melbourne, Australia 25-29 November 2000.**
Information: ICMS Pvt.Ltd. 84 Queensbridge Road, South Bank, Victoria Australia 30006

Break through to freedom

Hoechst Marion Roussel
Leading the way in allergy treatment

Once daily
allegra™
fexofenadine HCl
for allergies

The truly non-sedating antihistamine

ANTIBIOTIC TREATMENT FOR ACUTE CORONARY SYNDROMES-FACT OR FICTION

Upendera Kaul, M.D, D.M, F.A.M.S, F.A.C.C; Balbir Singh, M.D., D.M.; Rakesh Sapra, M.D., D.M.

Acute thrombotic occlusion (total or sub-total) is a very important central component in most acute coronary syndromes. It is therefore very logical that thrombus has become the fundamental target for therapy and prevention of both unstable angina and acute myocardial infarction. The genesis of coronary thrombosis as a mechanism of disease rather than a self limiting step in the process of vascular repair would thus open a number of additional modes of therapy of these syndromes.

The genesis of a thrombus in the vessel can be explained on the basis of two types of stimuli. (A) formation in response to pure mechanical forces at the site of an atherosclerotic plaque. The size of the thrombus in this case in determined by the thrombogenecity of the fissure. (B) An inflammatory activation of the vessel wall. In this situation growth and size of the thrombus is proportional to the intensity and duration of inflammation.

These two causes can co-exist and are not mutually exclusive. The additional pivotal role of the local vasoconstrictor response and the haemostatic mechanism is also well known[1]. The inflammatory cytokines by altering the properties of the vascular endothelium can abolish or diminish nitric oxide production leading to dimunition or cessation of its anti-thrombotic and vasodilator properties. They can also directly promote thrombosis, vasoconstriction and activation of metallo proteases, increase vascular permeablity, cause detachment of endothelial cells and digestion of intracellular matrix leading to the lysis of the cap of vulnerable plaques at their thinnest site[2].

The majority of thrombi are largely composed of platelets and not red cells and fibrin. This implies their gradual formation in response to weak but persistent thrombogenic stimuli. In acute coronary syndromes such thrombi are often multiple, multilayered suggesting a multiplicity and repeated recurrent thrombogenic stimuli. Thus a diffuuse and recurring inflammatory reaction couuld be a very plausible stimulus for thrombus formation. This would also explain the well known fluctuation in instability over a period of days in a large number of patients with unstable angina.[1]

Role of Inflammation

Data from histological studies has shown the presence of inflammatory cell infiltrates underneath acute coronary thrombi with or without plaque fissures in patients with unstable angina. Such infiltrates are also seen in plaques found in stable patients. This suggests that inflammation under some conditions could contribute to the development of atherosclerosis and in certain circumstances may cause acute activation of the vessel wall with resultant local thrombosis and vasoconstriction. Plaque fissuring may or may not be an association[3].

The pathogenetic role of inflammation is additionally supported by the independent prognostic value of inflammatory markers such as C-reactive protein. However only 50-70% of patients with class IIIb unstable angina (Braunwald's classification) have elevated values of C-reactive protein.[4,5]. The percentage of patients with elevated C-reactive protein on admission increases to 90%in patients in whom myocardial infarction was preceded by unstable angina, but decreases to 30% in patients in whom acute myocardial infarction was totally unheralded. Thus an acute inflammatory reaction detected systemically is present in a large number of patients with acute coronary syndromes but not detectable in all.

The inflammatory component may be the final common result of a variety of inflammatory stimuli, non-infectious and the response in an individual could be immunological and inflammatory.

Role of ChronicInfections & Inflammatory Markers

Chronic infections and their reactivation are possible inflammatory stimuli and there is some evidence that they may be associated with either the pathogenesis of atherosclerosis and/or precipitation of acute coronary syndromes[6-8]. Sero positivity for Helicobacter pylori and Cytomegalo virus has been reported to be higher in patients with atherosclerotic clinical syndromes than in controls[9]. Chlamydia pneumoniae also appears to be a possible infectious agent associated with the development of atherosclerosis[10]. The evidence linking this association rests both on indirect observation such as reduction in cardiovascular events coinciding with widespread antibiotic use[11] indirect serological[12,13] and in pathological studies[14] as well as on experimental animal models of C. penumoniae induced atherogenesis[15,16]. However these findings have not been confirmed by others[1]. Some studies have reported seropositivity for C. pneumoniae in upto 60% patients with unstable angina but a high incidence of this finding has been reported in controls.[17] Moreover the serological findings were reported to have a weaker correlationship as compared to C-reactive protein levels.

Thus although seropositivity for infectious agents appears correlated to a variable extent with atherosclerotic manifestations some patients with atherosclerotic manifestations and with acute coronary syndromes are seronegative and many seropositive individuals have non cardiac diseases and many apparently healthy controls are sero positive. There is thus need for a lot more research into the determinants of organ targetting of inflammation and the immune and inflammatory responses to possible infectious and non-infectious triggers.

Role of Macrolide Antibiotics

The available data on this subject suggests that macrolide antibiotics like roxithromycin used in a dosage of 150 mg twice daily for periods upto 30days in acute coronary syndromes especially non Q wave syndrome may have a beneficial effect on reduction of triple end points like death, acute myocardial infarction and recurrent ischaemia[18]. The study of Gupta et al[19] which showed long term benefits possibly suggests efficacy due to anti infectious effect. However Roxis study[19] and the data of Gurfinkal et al[17] which have shown benefits at 30 days but not at six months suggest efficacy due to an anticytokine effect rather due to antimicrobial effect. The results of the study of Gupta et al[19] using azithromycin in a one or two day cycle in patients seropositive for chlamydia showing benefits lasting up one year have not been reproducible in other studies. These discrepancies could be because of different inclusion criteria (only 50% patients in Roxis study were sero positive for Chlamydia).

Although the results of the trials on this subject conducted till date are not conclusive but they do raise a possibility of improving the average prognosis of acute coronary syndromes with antibiotic treatment. A study with atleast 4000 patients enrolled should have the 80% statistical power to get an answer[18]. Two important questions which remain unanswered are: (1) What are the actual mechanisms of the preventive effect of macrolide antibiotics? (2) Does the benefit appy to all patients with acute coronary syndrome?

Mega trial based evidence that post myocardial infarction patients benefit from beta blockers, aspirin, statins and ACE inhibitors already exists. Will antibiotics join this list? The final answer is yet to come from evidence based medicine.

Prof. Upendra Kaul M.D., D.M.
Director, Interventional Cardiology
Batra Hospital & Medical Research Centre
1, Tughlakabad Institutional Area
Mehrauli Badarpur Road, New Dehi (India)
JK-Practitioner 1999; 6(3): 179-181

References:

1. Maseri A. Ischaemic Heart Disease. A rational basis for clinical practice and clinical research. New York: Churchill Livingstone, 1995.237-301.
2. Libby P. Molecular bases of the acute coronary syndromes. Circulation 1995; 91:2844-50.
3. Van der Wal AC, Becker AE, Koch KT et al. Clinically stable angina pectoris is not necessarily associated with histologically stable atheroscilerotic plaques. Heart 1996; 76: 312-16.
4. Liuzzo G, Biasucci LM, Gallimore JR et al. Prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 1994; 331:417-24.
5. Rebuzzi AG, Quaranta G, Liuzzo G et al. Incremental prognostic value of serum levels of troponin T and C-reactive protein on admission in patients with unstable angina. AMJ Cardiol 1998; 82: 715-9.
6. Danesh J, Collin R, Peto R et al. Chronic infections and coronary heart disease: is there any link? Lancet 1997; 350:430-6.
7. Ellis EW. Infections and coronary heart disease. J Med Microbiol 1997; 46:535-9.
8. Gura T. Infections: a cause of artery-clogging plaques? Science 1998;281 (5373):35.
9. Liuzzo G, Caligiuri P, Grillo RL et al. Helicobacter pylori and cytoomegalovirus infections are strongly associated with the atherosclerosis but are not responsible for instability of angina (Abstr). J Am Coll Cardiol 1997;29:S2-217A.
10. Shor A, Kuo CC, Patton DL et al. Detection of chlamydia pneumoniae in coronary arterial fatty streaks and atheromatous plaques. S Afr Med J 1992; 82:158-61.
11. Anestad G, Scheel O, Hungnes O. Chronic infection and coronary artery disease. Lancet 1997; 350: 1028.
12. Saikku P, LeinonenM, Mattla K. Serological evidence of an association of a noval chlamydia, TWAR with chronic coronary heart disease and acute myocardial infarction. Lancet 1998; jii: 98-5.
13. Gurfinke E, Rozlosnik J, Bozovich G, Duronto E, Dos Santos A, Mautner B. IgG Antibodies to chlamydial and mycoplasma infection pluc C-reactive protein related to poor clinical outcome in unstable angina. Arch Inst Cardiol Mex 1997; 67:462-8.
14. Muhlestein JB, Hammond EH, Carlquit JF et al. Increased incidence of Chlamydia species within the coronary arteries of patients with symptomatic atherosclerosis versus other forms of cardiovascular disease. J Am Coll Cardiol 1996;27: 1555-61.
15. Fong IW, Chiu B, Vira E, Fong MW, Jang D, Mahony J. Rabbit model for Chlamydia pneumoniae infection. J Clin Microb 1997;35: 48-52.

16. Muhlenstein JB, Andersen JLL, Hammond EH et al. Infection with Chlamydia pneumoniae accelerates with development of atherosclerosis and treatment with azithromycin prevents it in a rabbit model. Circulation 1998;97: 633-6.
17. Gurfinkel E, Bozovich G, Daroca A et al. Randomised trial of roxithromycin in non Q wave coronarysyndromes: ROXIS Pilot Study. Lancet 1997; 350:404-7.
18. Gurfineel E, Bozovich G, Beck E al al. Treatment with the antibiotic roxithromycin in patients with acute non Q wave coronary syndromes. The final report of the ROXIS study. Eur Heart J 1999; 20: 121-7.
19. Gupta S, Leatham EW, Carrington D et al. Elevated Chlamydia pneumoniae antibodies, cardiovascular events, and azithromycin in male survivors of myocardial infarction. Circulation 1997; 96: 404-7.

Conference Calendar

INTERNATIONAL CONFERENCE ON "RECENT ADVANCES IN MEDICINE - AN UPDATE"

at Sher-i-Kashmir International Convention Complex
(Centuer Hotel), Srinagar, Kashmir
on
August 21-22-1999

For details contact:
Prof. G. M. Malik
Organising Secretary
Prof. of Medicine SMHS Hospital, Srinagar
P.O. Box: 884, GPO, Srinagar, 190 001, Kashmir, India
Fax: 091-194-455592 (R) 0194-453115 (O)
Phone: 091-194-432060 (R) 0194-452013 (O)
E.Mail: zakhatib@nde.vsnl.net.in

International Congress on Atherosclerosis, Hypertension and Coronary Artery Disease and Annual Conference of Indian Society of Hypertension at New Delhi on October 14-16, 1999

for further details and registration contact:

Dr. H. S. Rissam
Organising Secretary
Escort Heart Institute and Research Centre, Okhla Road, New Delhi - 110025, India, Fax: 91-11-6825013

ACUTE LIVER FAILURE

Mohammad Sultan Khuroo, MD. DM. FACP. FRCP (Edin)

Acute liver failure (ALF) is a dramatic and challenging syndrome in clinical medicine. Although an uncommon disorder, it is usually fatal. At present there is no universally accepted criteria for diagnosis of ALF. However, for practical purposes, it is defined as the cocurrennce of encephalopathy in a previously healthy person, within six months from onset of severe liver disease[1,2]. This syndrome is subdivided into fulminant hepatic failure, if onset of encephalopathy is within eight weeks, and late onset hepatic failure, if the onset of encephalopathy is 8-24 weeks from the onset of liver disease. The definition usually includes the absence of pre-existing liver disease, however, ALF may be the presentation of Wilson's disease, autoimmune chronic active hepatitis, and chronic hepatitis B infection[3-7]. ALF has been subdivided into a number of syndromes by various investigators, based on the duration between onset of jaundice to onset of encephalopathy (Table I)[8-13]. These syndromes differ from each other in etiology, disease course, complications and survival, and should help in defining treatment strategies. Hepatic encephalopathy of ALF must be differentiated from hepatic encephalopathy in patietns with chronic liver-disease, the so-called portosystemic encephalopathy (Table-2)[14,15].

Epidemiology

There is little information on the epidemiology of ALF in various regions of the world. Crude estimates suggest that there are approximately 2000 deaths per year from ALF related to viral hepatitis in the United States[1]. In contrast, ALF caused by hepatitis E is a national health problem in the developing countries. Hepatitis E causes large-scale epidemics of hepatitis in the Indian subcontinent, involving hundreds of thousands of cases with high mortality[16].

Etiology

ALF can result from diverse etiology agents (Table-3).[17,18] Of these, hepatitis viruses, acetaminophen overdose and idiosyncratic drug reactions constitute the bulk of cases. Metabolic and vascular liver diseases (Figure-1), liver diseases unique in pregnancy (Figure 2) and a number of miscellaneous liver diseases causes a small number of the remaining cases.

Acetaminophen

The most common cause of ALF in the United Kingdom is related to acetaminophen toxicity in association with a suicidal oor parasuicidal episodes[19,20]. Hepatotoxicity has been reported after therapeutic doses in patients who are concurrently taking enzyme-inducing drugs, such as phenytoin, and in patients who are chronic consumers of alcohol. Alcohol acetaminophen syndrome is emerging as an important cause of ALF in the United States. The syndrome is characterized by extremely high transaminase levels and a poor prognosis[21,22].

Viral Hepatitis

Hepatitis A is a relatively uncommon cause of ALF. This is due to the benign course of illness caused by this agent, with case fatality rates of around 0.1%-0.4%[1,14] Hepatitis E is the most common cause of ALF in endemic regions of the world, with high mortality (25%) in pregnant women (Figure 3)[23-26]. Hepatitis B has a case fatality of around 1.0% and constitutes a significant percent of ALF in various endemic regions of the world.[1,13]. Chronic hepatitis B can cause ALF during reactivation, especially after immunosuppression therapy[6]. Moreover, in about 50% of patients with ALF and chronic hepatitis B positive status. ALF is precipitated by another factor, usually superinfection with hepatitis D virus, hepatitis E virus, or putative non-A-E agent[7]. Hepatitis C is a very rare cause of ALF in Europe and the United States[27,28], although a number of series from Japan and India have found evidence of hepatitis C in the non-A, non-B group of patients[24,25,29]. The etiology of ALF is unknown in 30%-50% of patients and is presumed to be caused by yet unidentified non-A-E viral agent. This non-A-E agent accounts for 90% of patients with late onset hepatic failure, and identification of this agent is a matter of great priority[30-31].

Hepatitis G virus is a newly identified positive-stranded RNA virus, with a genome of 10 KB, and belonging too the member of the Flaviviridae, distinct from hepatitis C virus. It has, though possibly prematurely, received the appellation of hepatitis virus.

JK-Practitioner 1999; 6(3): 182-190
Reproduced with permision of Prof. Mohd Sultan Khuroo From Annals of Saudi Medicine 1998;18:318-326

Table 1. The various syndromes of acute liver failure and their characteristics.

	Acute hepatic failure		Hepatic failure				
Characteristics	Fulminant hepatic failure	Late onset hepatic failure	Hyperacute	Acute	Subacute	Fulminant	Subfulminant
Pre-encephalopathy icteric period	≤8 weeks	8-24 weeks	≤ 1 weeks	1-4 weeks	5-12 weeks	≤2 weeks	2-12 weeks
Cerebral edema	Common	Unusual	common (69%)	Common (56%)	Unusual (14%)	Common	Less common
Ascites, renal failure	Unusual	Common	Unusual	Unusual	Common	Unusual	Common
Etiology	HV/paracetamol	Non-A-E	Paracetamol	Non-A-E	Non-A-E	HV/drugs	Non-A-E
Survival	Moderate (20%-30%)	Poor(<10%)	Moderate (36%)	Poor (7%)	Poor(14%)	Moderate (30%)	Poor (10%)

The clinical implications of hepatitis G virus in causing acute and chronic liver disease are as yet unclear. Of significance are the data that the vbirus has not been implicated in the etiology of ALF caused by putative non-A-E agent[32]. However, in one study, a specific strain of the virus was detected in a high precentage of German and Japanese patients with ALF. These results, though interesting, need to be confirmed by other workers[33].

Drug Reactions

Idiosyncratic drug reactions resulting in ALF include a wide variety of drugs Some of the common agents associated with ALF are non-steroidal anti-inflammatory drugs and antitubercular drugs. Of perhaps greater concern than single agents is the use of drug combinations which result in ALF[2]. These include trimethoprim-sulfamethoxazole; amoxicillin-calvulanic acid (Augmentin), rifampicin-isoniazid and isoniazid acetaminophen.

The dominant etiologic agents of ALF have wide geographic variation[16,17]. Viral hepatitis is nearly the sole agent of ALF in the Indian subcontinent, the most important cause in Europe and the United States, and comes next to acetaminophen hepatoxicity as a cause of ALF in the United Kingdom.

Clinical Features

Clinical features of ALF can be divided into two broad groups: 1) manifestations of acute hepatic injury, namely, jaundice, shrunken liver, high liver enzymes, deficiency of cloting factors and other synthetic functions of the liver; and 2) multiorgan failure and a wide range of metabolic disturbances.[2,17]

Encephalopathy

Encephalopathy is the essential clincial feature of ALF, and is graded on a scale of 1 to 4.[15] The grade of encephalopathy has prognostic value and patients with grade 2 encephalopathy, without further progression, have an excellent prognosis. In contrast, patients with grade 3 or 4 coma carry a poor prognosis[2,13-15]

Table 2. The differentiating features of encephalopathy in acute liver failure and chronic liver disease (portosystemic encephalopathy)

	Acute liver failur	Portosystemic encephalopathy
Encephalopathy	Sudden, progressive	Grandual, fluctuating
Cerebral edema	Yes	No
Liver disease	Acute (massive necrosis /fatty liver)	Chromic (cirrhosis)
Porto-systemic shunts	No	Yes
Multiorgan failure	Common	Unusual
precipitating events	No	Common, usually multiple like GI bleed, infection, drugs, electrolytes imbalance, etc.
Treatment	Intensive care, liver transplantation	Treat precipitating events/lactulose)
Outcome	Poor (20%)	Good (≥ 90%-100%)

Cerebral Edema

Cerebral edema is one of the most important causes of death in ALF. The pathogenesis of cerrebral edema is unclear and may be caused by vasogenic (direct leakage of plasma into the cerebrospinal fluid) or cytotoxic (cellular injury causing increased water uptake) mechanisms. The early clinical signs of cerebral edema are subtle and include changes in pupillary response, bradycardia, hypertension and hyperventilation. Changes in muscle tone, myoclonus, seizures and decerebrate rigidity follow, and may occur upredictably fast to cause respiratory arrest or irrevrsible brain damage.[34] The management of cerebral edema needs a few simple measures. It has been observed that tactile stimuli, faulty neck position and physical manipulation can precipitate episodes of cerebral edema. Thus patients with ALF need to be nursed in a quiet room, with the head end of the bed elevated, and institution of early mechanical ventilation and muscle paralysis with onset of grade 3 encephalopathy. A high clinical index of suspicion of cerebral edema should be kept and early warning signs detected by careful monitoring. Direct measurement of intracranial pressure is a valuable tool to diagnose and monitor response to therapy in such patients. Intracranial pressure monitoring is indicated in all patients with grade

Table 3. The etiological courses of acute hepatic failure

Broad group	Subgroup	Agents
Hepatitis viruses	Enteric	HAV
		HEV (endemic zones) HDV Coinfection (Drug addicts) superinfection (edemic zones) HCV (some geographical regions only)
	Undefined/unknown	Non-A-E (most common cause globally)
	Others	CMV, herpes (immunocompromised person)
Overdose/ toxins	Acetaminophen	Acetaminophen overdose alcohol-acetaminophen syndrome, acetami--nophen-phenytoin syndrome.
	Amanita phalloides Bacillus cereus toxin	
Idiosyncratic drug reactions	Single agents	Isoniazid, NSAID, valproate, sulfonamides, L-asparaginase.
	Drug combinations	Amoxicillin-clavulanic acid, trimethaprim-sulfamethoxazole, rifampicin-isoniazid
Liver disease in pregnancy	Unique to pregnancy	Acute fatty liver of pregnancy, HELLP syndrome, hepatic infarc tion, subcapsulr hematoma.
	Intercurrent	Hepatitis E, Budd-Chiari syndrome
Vascular disease of liver	Ischemic hepatitis	Shock, cardiac arrest, CCF with low output
	Outflow obstruction	Budd-Chiari syndrome, veno-occulsive disease.
	Post-liver transplant	Hepatic artery thrombosis; graft non-function.
Metabolic disease of liver		Wilson's disease, Reye's syndrome
Miscellaneous		Hepatic resections, hyperthermia, fatty liver, lymphoma, autommune chronic acute hepatitis

Table 4. Steps of management of acute liver failure.

1. Diagnosis:
   Acute live disease
   Prolonged prothrombin time (>5 sec.)
   Altered mentation
2. Treat specific causes;
   Pregnancy
      Delivery
   Acetaminophen
      N-acetylcysteine
   Amanita phalloides
      Penicillin and silibirin
   Wilson's
      Chelation
   AICAH
      Steroids
3. Intensive care
   Clinical/Laboratory monitoring
   Prophylactic antibiotics
   H_2 receptor antagonists
4. Assess severity:
   Bad prognosis
      Ventilation
      ICP monitoring
      Liver transplantation.

3 or 4 encephalopathy and those being considered for liver transplantation. The procedre is hazardous and needs experienced hands, and prior correction of coagulopathy by fresh frozen plasma and/or platelet transfusion.[35] A standardized approach to treat episodes of cerebral edema includes: 1) hyperventilation to keep pCo_2 les than 25 mm Hg, if no response, 2) administration of mannitol (0.5 to 1 g/kg) as a bolus intravenously, which can be repeated if needed in case there is no response; 3) maintaining serum osmolality between 310 to 320 mOsm/L and monitoring urine flow to ensure diuresis. In patients with oliguria, mannitol is administered along with ultrafiltration to remove fluid and to prevent worsening of cerebral edema. If there is no response to mannitol, or if cerebral edema relapses, thiopental sodium coma can be induced, using a bolus of 3 to 5 mg/kg of the drug intravenously and followed by intravenous infusion at a rate of 50-250 mg/h for the next 4 hours[34].

Coaglopathy

ALF results in wide qualitative and quantitative defects in platelets, coagulation factors and the fibrinolytic system. Disseminated intravascular coagulation may also play a role, although this syndrome is difficult to distinguish from changes due to failure of hepatic synthesis of coagulation factors and their clearance alone. Prothrombin time is a good guide to prognosis. The coagulopathy presents as bleeding, which may be severe, and may cause or contribute to death in around 30% of patients. The most common site of bleeding is the upper gastrointestinal tract, possibly precipitated by the occurrence of gastric erosions, in addition to coagulopathy. Other important sites of bleeding include the nasopharynx, lungs, kidneys, retroperitoneum and skin (if punctured). H_2 receptor antagonists and sucralfate therapy can reduce incidence of gastrointestinal bleeding and improve survival, independent of correction of coagulation factors. Management with blood products is indicated only in manifest bleeding, or to cover periods during invasive procedures.[36]

Infections

Patients with ALF have increased susceptibility to infections as a result of impaired phagocytic function, reduced complement levels, and the need for invasive procedures. Bacteriologically proven infection is recorded in up to 80% of these patients, and fungal infections (predominantly Candidiasis) in 32%. The predominant bacterial pathogens include Staphylococci aureus, coagulase-negative Staphylococci, Streptococci

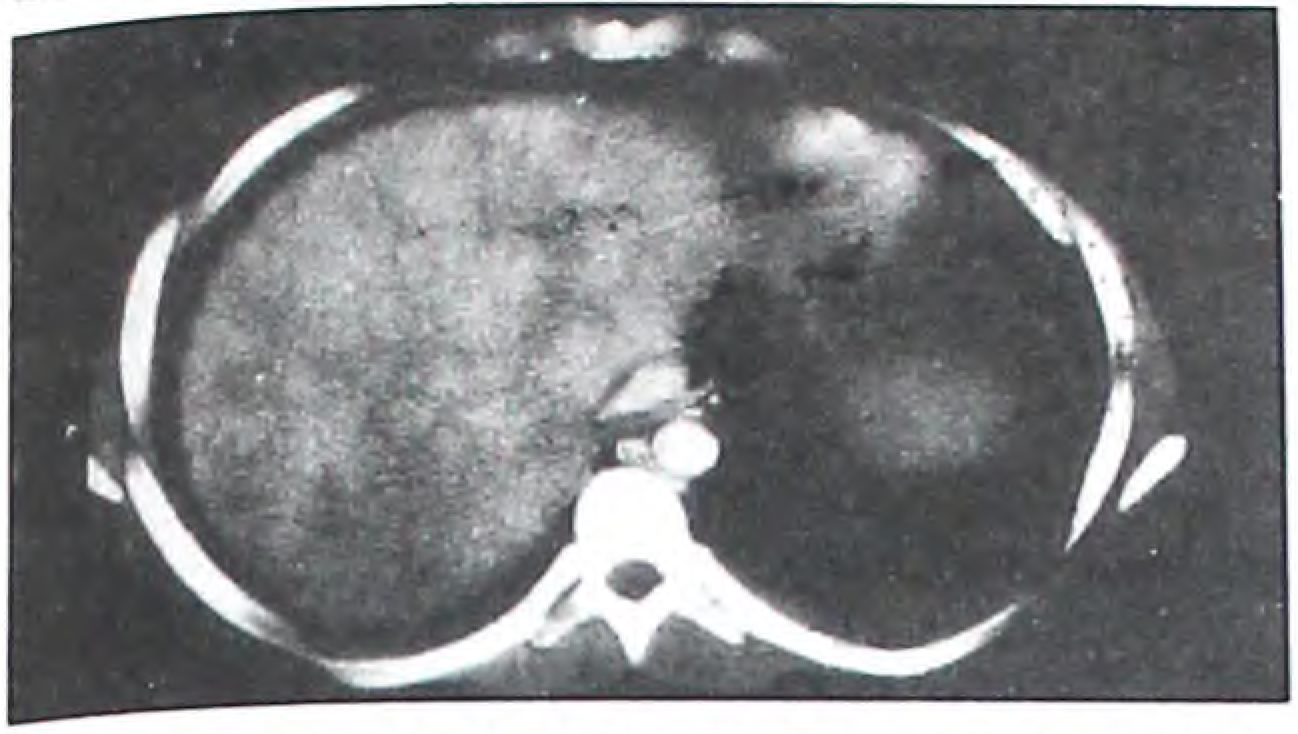


FIGURE IA. Acute liver failure caused by hepatic vein thrombosis. This 30 year-old woman developed abdominal pain, ascites, jaundice and progressive encephalopathy during 36 weeks of her pregnancy. She died with massive gastrointestinal bleeding and cerebral edema two weeks after the onset of her illness. Abdominal computed tomographic scan after oral and intravenous administration of contrast medium, showing extensive hypodense areas suggestive of hepatic congestion.

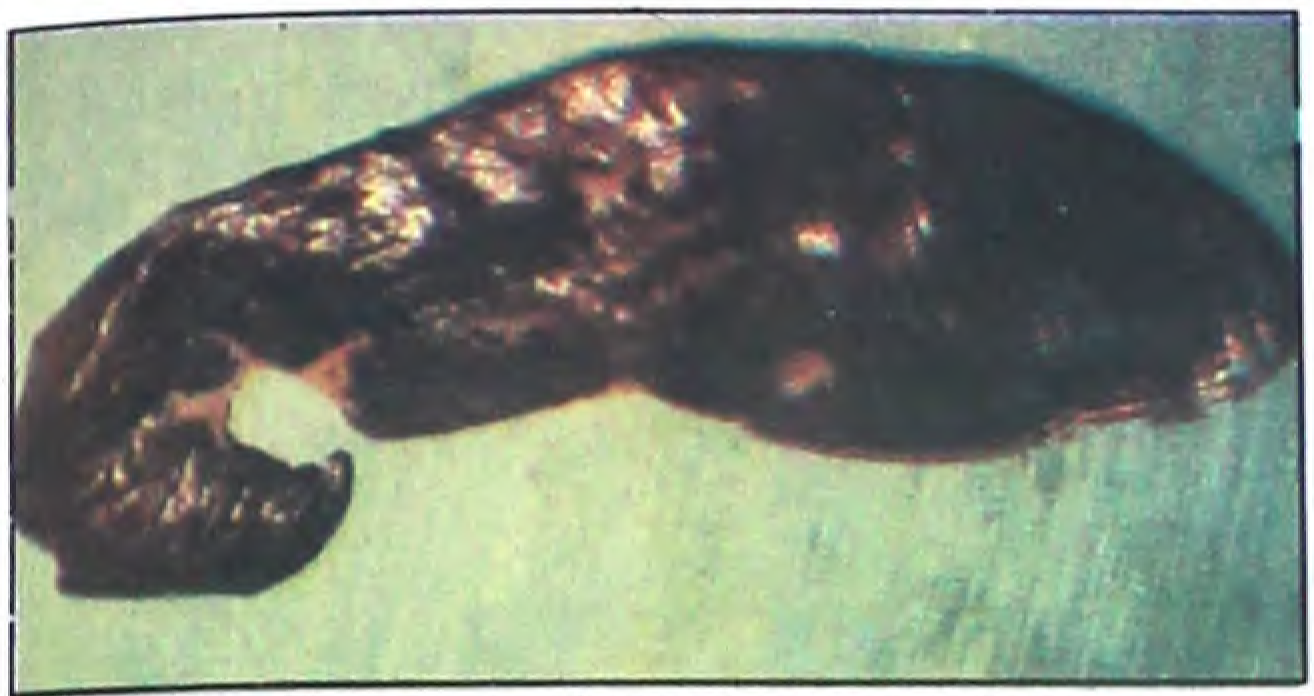


FIGURE IB. Photograph of sliced liver at autopsy revealing extensive hemorrhage in the liver parenchyma.

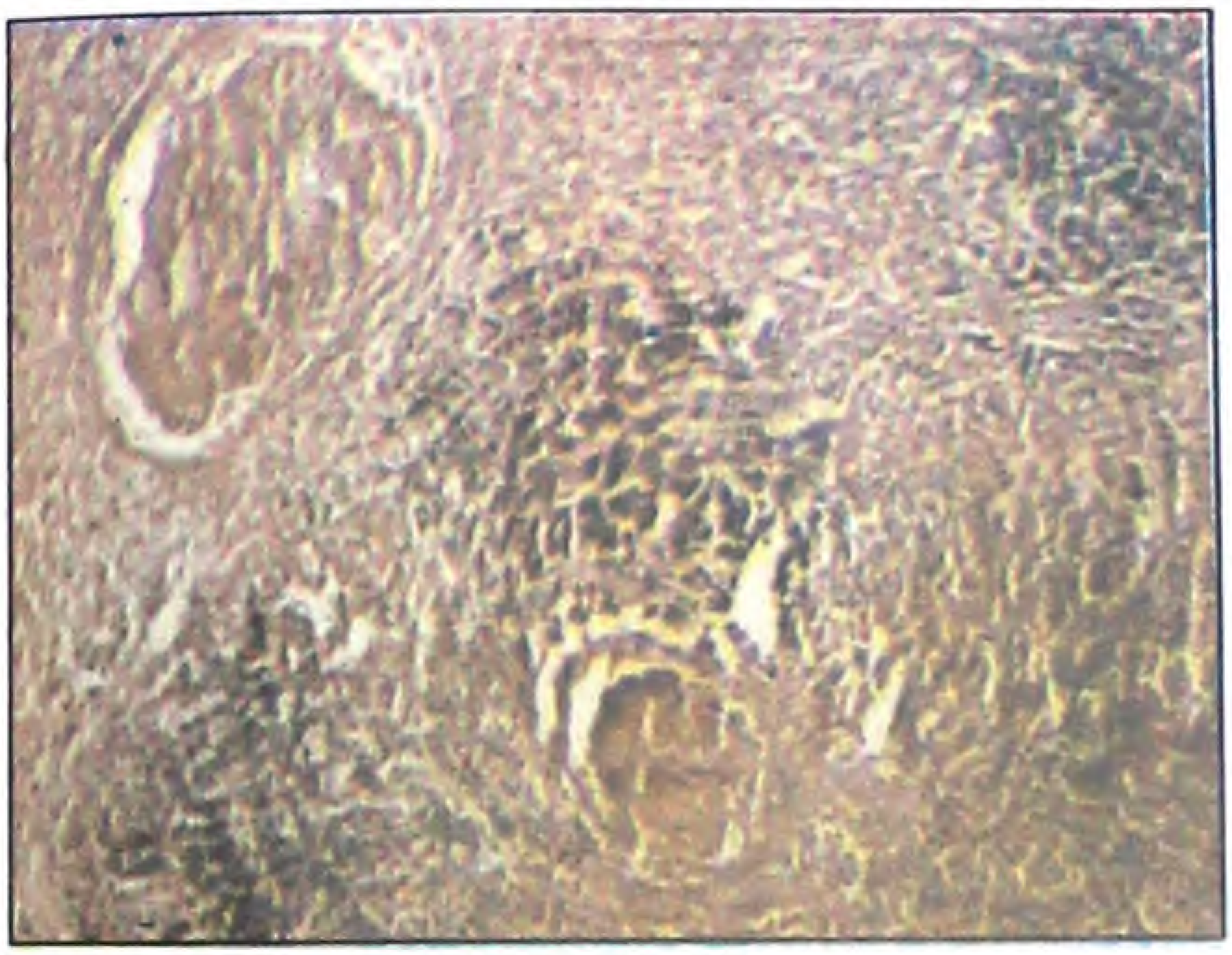


FIGURE IC: Micrphotograph of liver revealed multiple thrombi in hepatic veins, extensive centrilobular hemorrhagic necrosis and a few islands of surviving liver cells.

Table 5 The clinical manifestations of acute liver failure and suggested treatment strategies

Manifestations	Prophylaxis	Treatment
Neurologic encephalopathy cerebral edema	ICU monitoring, ICU monitoring, ventilation	$PCO_2 < 25$ mm Hg. mannitol thiopental
Coagulopathy	Vit K IV, H_2 receptor antagonists correct prothrombin time prior to procedures	Fresh frozen plasma/ platelets only if manifest bleeding
Infections	Daily cultures, prophylaxix (ceftriaxone + flucloxacillin + oral amphotericine B)	Culture +Ve use antibiotics on sensitivity, sepsis suspected (Culture-Ve) vancomycine + imipenem, if no respnse, add amphotericine B
Metabolic	Check blood glucose every every hour, check serum electrolyte as required	IV glucoseif blood sugar ≤3.5 mmol/L, correct electrolytes as needed
Hemodynamic	Maintain PWP >12 mmHg dopamine IV 3-5 mg/kg/ min.	Human albumin 5% IV bolus/infusion, vaspressors /N-acetylcysteine/PGE2

species and coliform organisms (Escherichia coli and Pseudomonas aeurginosa). The usual sites of infections include chest, urinary tract, blood and intravenous cannulae[37]. Spontaneous bacterial peritonitis is common in patients with late onset hepatic failure, and occurred in 32%f of 82 patients in one study[38]. Clincial signs of sepsis, such as high temperatue and high leukocyte count, are absent in 30% of cases. Use of prophylactic antibiotics in patients with ALF causes significant decrease in bacterial infections, shortens hospital stay, increases rate of successful liver transplantation and improves overall survival. As usual clinical signs of sepsis may be absent, careful monitoring by regular cultures is important to detect infections early[37-39].

Metabolic Changes

ALF is associated with a number of metabolic changes. Hypoglycemia is common and may precede the onset of grade 3 encephalopathy, resulting in precipitous deterioration in mental state. The hypoglycemia is a consequence of increased circulating insulin levels, impaired gluconeogenesis and inability to mobilize glycoogen stores. The clinical signs and symptoms of hypoglycemia are masked in the presence of established encephalopathy, and blood glucose monitoring should be done on an hourly basis and supplement glucoose administered intravenously when blood glucose administered intravenously when blood glucose falls below 3.5 mmo/L.[40]

Hyperventilation occurs early in the course of ALF, causing respiratory alkalosis even before grade 3 coma ensues. In addition, hyponatremia, hypokalemia,

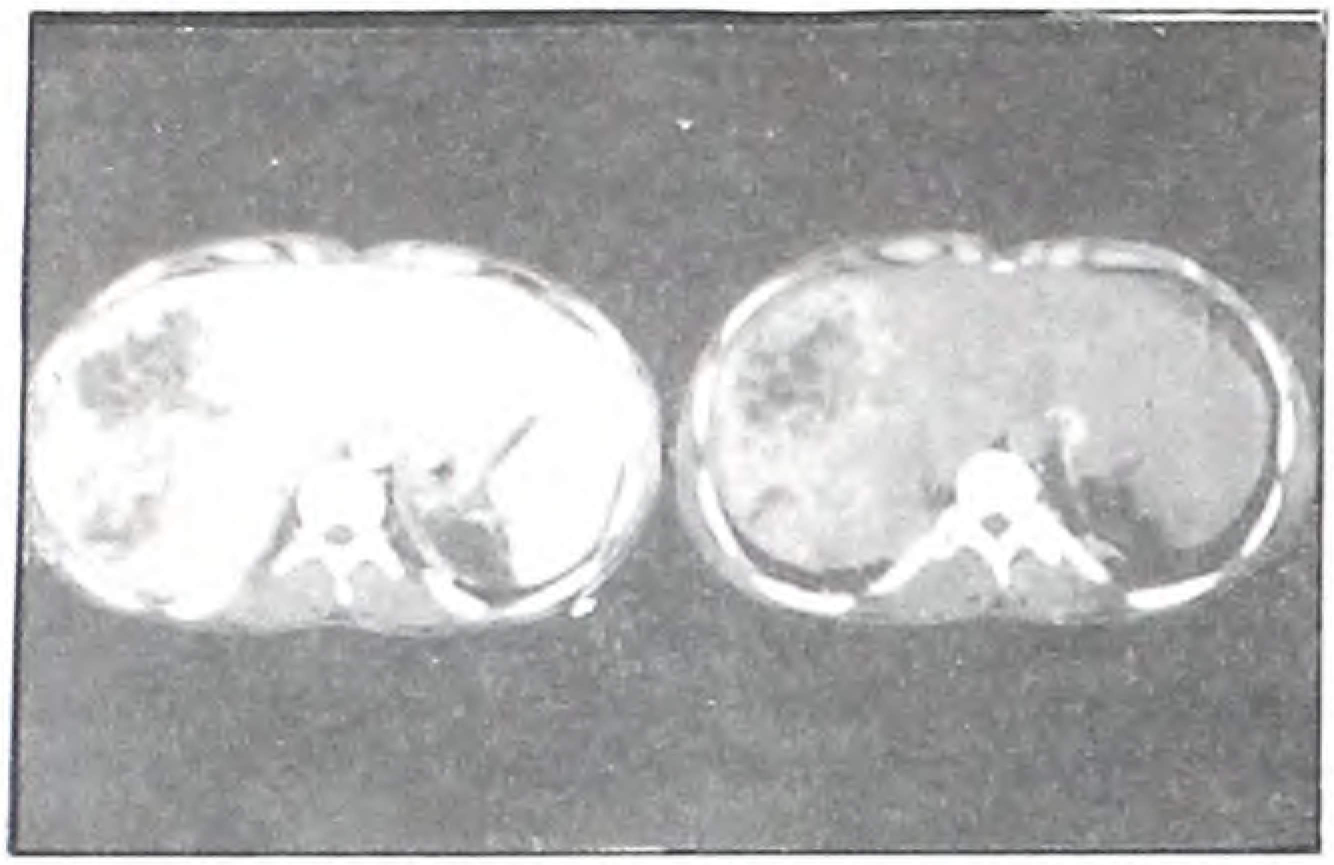


FIGURE 2 A: Acute liver failure caused by hepatic infarction in a pregnant woman. Abdominal computed tomographic scan: nonenhanced scan (right panel) revealed a large hypodense area in the right lobe of liver with irregular hyperdense area around the lesion suggestive of cxalcification. The contrast enhanced scan (left panel) revealed the large hypodense lesion with marked contrast enhancement of the surrounding liver.

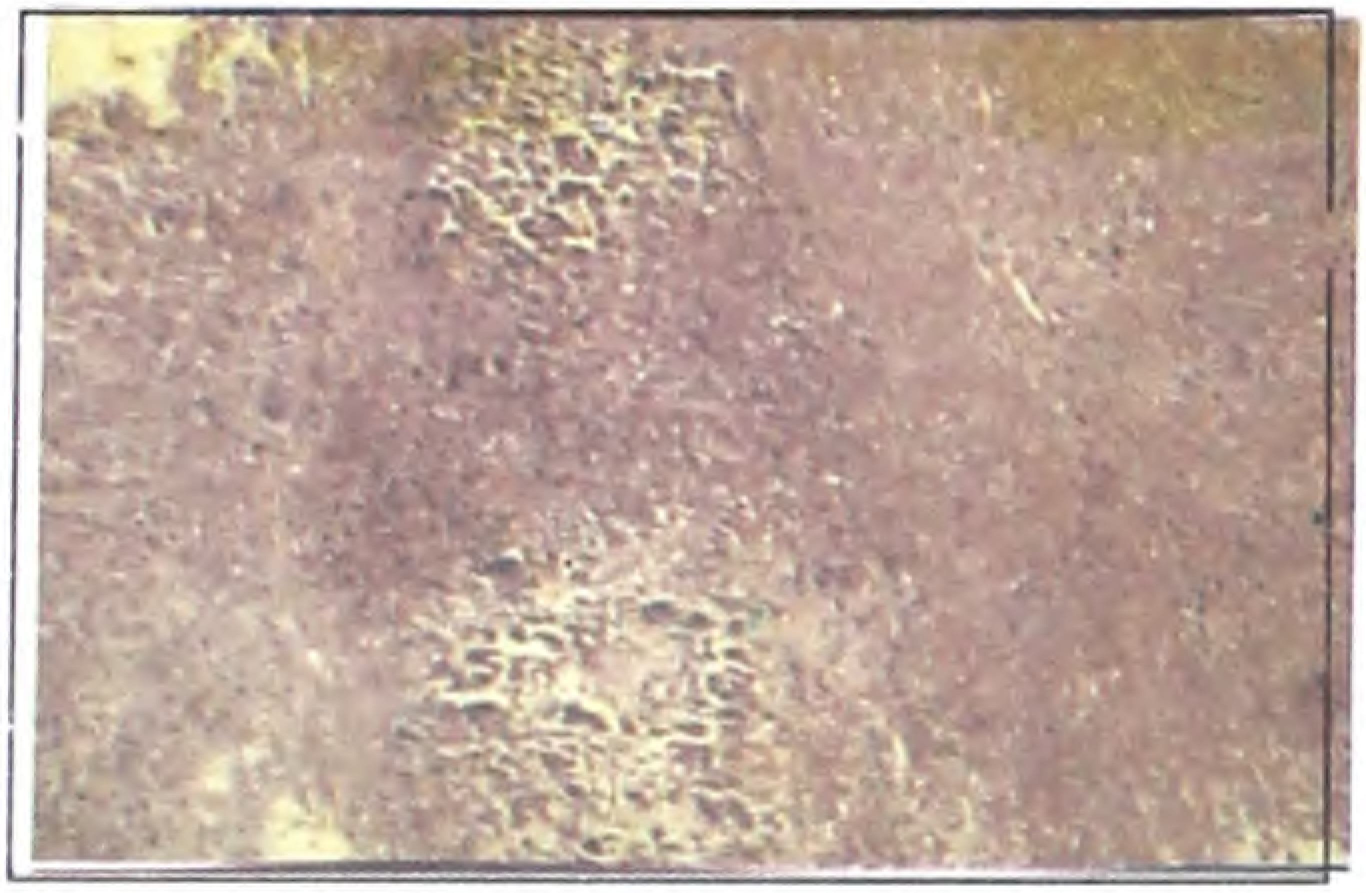


FIGURE 2B : Microphotograph of needle biopsy of liver revealing extnesive areas of hepatic infarction with two foci of parenchymal calcification.

hypophosphatemia, and hypomagnesemia occur frequently, and need regular monitoring and correction. However, acetaminophen-induced ALF can lead to metabolic acidosis in a high percentage of patients early in the clinical course of overdose, and precedes onset of encephalopathy.[17]

Hemodynamic Changes

Circulatory changes resembling septic shock syndrome occur in ALF, and are a result of release of toxic substances from tissue injury and cytokines from activated macrophages[41]. ALF is associated with abnormal oxygen supply dependency pattern resulting in oxygen extraction taking place over a wider than normal range of oxygen delivery. Severe peripheral shunting occurs and tissue oxygen extraction is diminished, leading tolactic acidosis. Prosptaglandins (PGE_1 and PGE_2) and N-acetylcysteine have been shown to increase tissue oxygen extraction and improve hemodynamics in such patients, however, whether such therapy can improve survival is not known.[42-44] Functional renal failure occurs in about one-third of patients with ALF, as a result of hypovolemia, sepsis and reduced intravascular filling pressures. Oliguric renal failure occurs late in the clinical course of the disease. In contrast, acetaminophen can cause direct renal toxicity, resulting in oliguric renal failure in around 75% of patients. Prevention of hemodynamic changes should be directed at maintaining vascular filling pressure by use of intravenous albumin infusions and aiming at a pulmonary wedge pressure of 12 to 13 mm Hg. Persistent hypotension with adequate intravascular volumes carry poor prognosis and can be managed by vasopressors. Conventional hemodialysis can lead to sudden changes in the circulatory volume and electrolyte balance and may worsen cerebral cdema. Thus continuous veno-venous hemofiltration is he preferred option. If not available, continous arteriovenous hemofiltration may be the next alternative following formation of a temporary shunt in the forearm.[17]

Table 6: Prognostic model developed at King's College Hospital to select patients with acute liver failure for liver transplantation

Acetaminophen overdose
- Atretial pH<7.3 or all three of following:
- prothrombin time > 100 sec.,
- creatinine > 300 umol/L,
- grade 3 or 4 encephalopathy

Other causes
- prothrombin time > 100 sec. or INR > 6.7 or any of the three of the following:
- unfavorable cause (non-A, non-B hepatitis, drug reaction);
- jaundice > 7 days before encephalopathy,
- age < 10 or > 40 years;
- prothrombin time > 50 sec or INR > 4;
- serum bilirubin > 300 umol/L

Table 7. Future developments for treatment of acute liver failure.

Artificial hepatic support system
Extracorporeal liver support
Hepatocyte transplantation
Xeno tranplantation

Management

Intensive Care

Management of ALF starts from the diagnosis of the syndrome in the emergency room (Table 4). Altered mentation and coagulopathy in a patient with liver disease are hallmarks of the diagnosis, and such patients need admission to the intensive care unit and appropriate monitoring.[1,2,9,13]

Specific Therapy

From therapeutic considerations, it is imperative to evaluate for etiologies which have specific treatments and/or antidotes (Table 5). ALF caused by HELLP syndrome, fatty liver of pregnancy and Budd-Chiari syndrome following pregnancy, need urgent termination of pregnancy.[45-47] Acetaminophen overdose should be treated with N-acetyl cysteine.[19,20] Nanograms of serum acetaminoophen levels to predict hepatotoxicity are of little value in alcohol-acetaminophen syndrome because of a number of reasons: 1) time of ingestion is frequently not available; 2) ingestion usually occurs over multiple stages; and 3) hepatotoxicity can occur with therapeutic doses and low blood levels in patients with concurrent use of alcohol.[2,21,22] Mushroom poisoning caused by the species Amanita phalloides needs urgent gastric lavage and penicillin 3000,000 to 1,000,000 units/kg/day intravenously in divided doses, plus silibinin (a water-soluble form of silymarin) 20 to 50 mg/kg/day intravenously.[14]

Metabolic diseases of liver, namely, Wilson's disease and autoimmune chronic active hepatitis, need specific therapies.[3-5,48] Hepatic venous outflow obstruction (Budd-Chiari syndrome) responds well to anticoagulation and urgent portacaval shunts performed at surgery, or through creation of a transjugular intrahepatic portosystemic shunt.[49-52]

Liver Transplantation

The successful use of liver transplantation has had the single greatest impact on the management of ALF.[1,53,54] The selection of patients, appropriate timing of the transplant, the difficulty of making donor liver available within a short period of time, and postoperative course of these sick patients make the transplantation for ALF a very challenging field. Over the years, ALF has constituted between 6% to 7% of total liver transplantation performed in the United States. ALF patients undergoing liver transplatntation were more likely to be younger, on life support (status 4), to receive incompatible blood systems, and have considerably shorter waiting time than those undergoing transplantation for other causes. In view of these disadvantages, patients with ALF had a lower one-year rate of patients (63%) and graft (53%) survival than patients transplanted for other causes (78% and 70%, respectively).[1,50] Liver transplant should be offered to patients with ALF before severe irreversible brain damage has ensued, and prior to performing the transplant a careful assessment of the brain function needs to be done to exclude irreversible brain damage.[17,53,54]

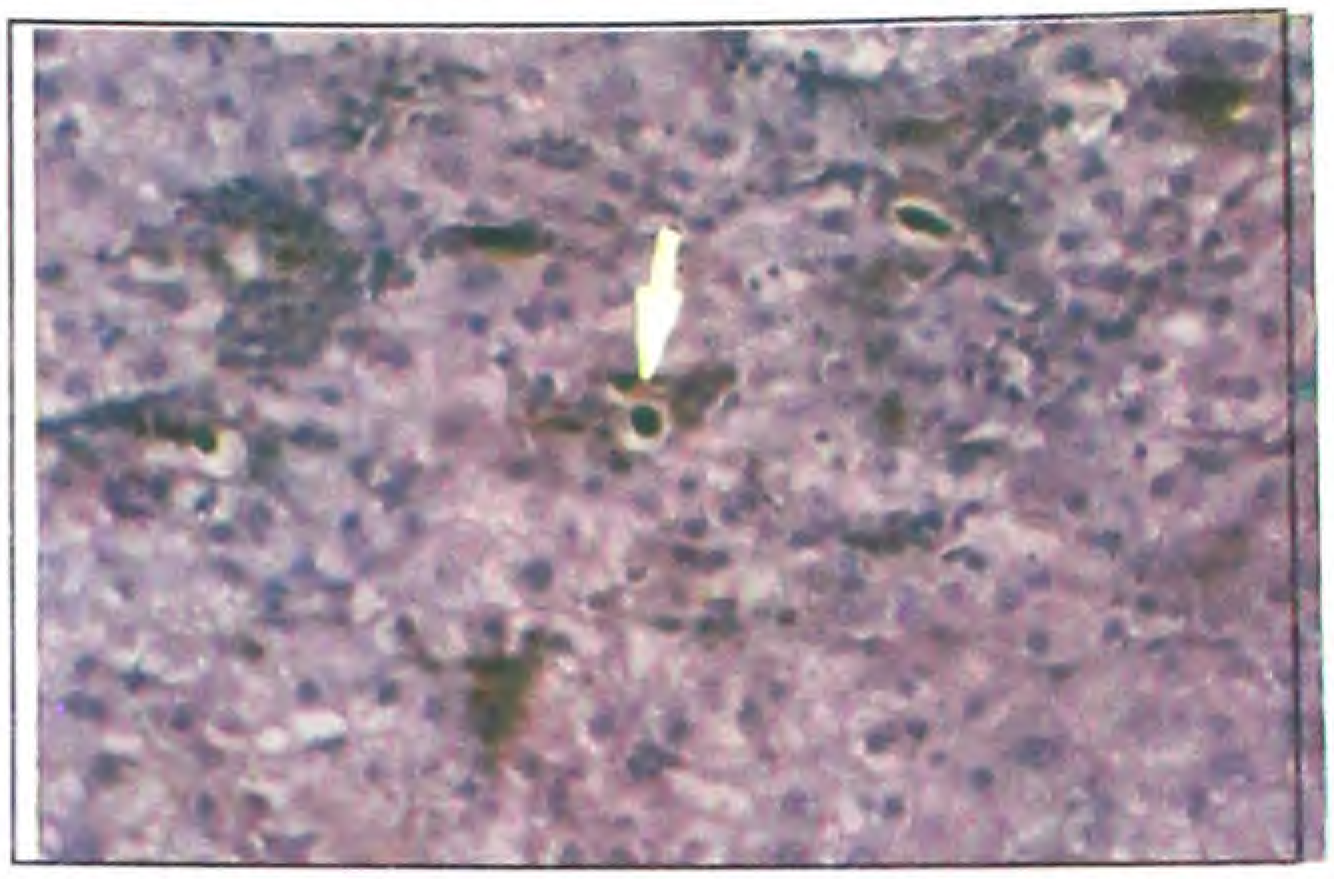


FIGURE 3, Microphotograph of needle biopsy of liver from a patient with acute liver failure caused by hepatitis E virus. This 25 year-old pregnant woman developed acute liver failure during the third trimester of pregnancy. Serum sample collected on her 10th day of illness was reactive for IgM antibody to hepatitis E virus (ELISA) and HEV RNA (PCR). Dominant changes in liver biopsy were panlobular marked intracanalicular cholestasis (bile plugs) with pseudo-ductular formation (arrow), focal necrosis and lobular disarray.

The majority of patients with ALF have received orthoptic liver transplantation, however, the possibility of eventual recovery makes auxiliary liver transplantation an attractive option. The advantages of auxiliary liver transplantation are temporary requirement of immuno-suppression drugs until the host liver recovers and the relative ease of surgery. Two types of auxiliary liver support are possible: heterotopic transplantation, in which the liver graft is placed in the right upper quadrant beside the native liver, and auxiliary orthopic liver transplantation, where the portion of native liver is removed and replaced by the reduced size graft.[55-59]

Prognostic Indicators

Critical in the decision to use liver transplantation is the assessment of the likelihood of spontaneous recovery. A number of transplant centers in the West have defined prognostic criteria in ALF, and these criteria can be applied to estimate the probability of spontaneous recovery in a given patient.[60-63] The criteria include static variables, such as age, sex and etiology, and dynamic variables, such as grade of encephalopathy, serum bilirubin, prothrombin time, etc. The prognostic model proposed by King's College Hospital in London is the most popular for reference.[60] This model divides ALF into two broad etiological groups, acetaminophen and non-acetaminophen. In the acetaminophen group, arterial pH of <7.3, prothrombin time of >100 sec., and serum creatinine of >300 mmol/L were bad prognostic variables. In the non-acetaminophen group, etiology (non-A-E agents or drugs), age (<10 or >40 years), pre-encephalopathy period (>7 days), serum bilirubin (>300 mmol/L), and prothrombin time (>50 sec.) were bad prognostic variables (Table 6). By contrast, French workers rely primarily on factor V levels, with a value of less than 20% (30% in those over 30 years), leading to transplantation. Factor V estimations were found to less sensitive but more specific than the King's College criteria when determined 48 hours before tranplantation. Recent data published from India have shown that these prognostic indicators may not be valid for other geographical regions, in view of the differences in the etiological causes, behavior and clinical profile of ALF.[25] Thus, such prognostic indicators need to be defined for different geographical regions and validated by application into prospective studies.[63]

Future Developments

In recent years, there has been considerable interest in the use of newer forms of support system or transplantation in patients with ALF that may provide a bridge until the native live recovers its functions spontaneously, or until an appropriate donor is available (Table 7).[63-98] Some of these developments may also address the issue of difficulty in finding a donor liver and use of alternative/innovative forms of transplantation.[1] Such approaches would avoid major surgery, allow use of liver related donors, have feasibility of multiple courses of treatments and could be used for temporary support without committing the patients to life-long immunosuppression.

Artificial hepatic support systems are cell-based extracorporeal system incorporating hepatocytes, which take up various excretory and synthetic hepatic functions until the liver regenerates.[64-68] Two bioartificial devices have already been used clinically in the treatment of ALF: bioartificial liver (BAL), based on pig hepatocytes attached to microcarriers, and the extracorporeal liver assist devices (ELAD), which contain a human liver-derived tumor cell line (C3A cells). Hepatocyte transplanttion uses hepatocytes rather than the whole organ for transplantation.[69-75] The procedure would be ideal for transfer of genes to individuals with genetic diseases, such as familial hypercholesterolemia, Griggler-Najjar syndrome, etc. Extracorporeal liver (ECL) support system involves the diversion of patient's circulation through a liver outside the body.[76,77] The organ used for cross-circulation may be human or from another species. Xenotransplantation uses baboon or pig liver to perform human hepatic functions. Anecdotal reports of the use of the above devices in humans with ALF appear in the literature, but such devices need further refinements to be evaluated by controlled clinicals trials for proper evaluation.[78]

References:

1. Hoofnable JH, Carithers RL Jr., Shapiro C, Ascher N. Fulminant hepatic failure: summary of a workshop. Hepatology 1995;21:240-52.
2. Lee WM. Acute liver failure. Am J MEd 1994;96(Suppl A):3-9.
3. Nazer H, Ede RJ, Mowat AP, Williams R. Wilson's disease: clinical presentation and use of prognostic index. Gut 1986;27:1377-81.
4. Walia BN, Singh S, Marwaha RK, Bhusnurmath SR, Dilawari JB. Fulminant hepatic failure and acute intravascular haemolysis as presenting manifestations of Wilson's disease in young children. J Gastroenterol and Hepatol 1992;7:370-3.
5. Maggiore G, Porta G, Bernard O, Hadchouel M, Alvarez F, Homberg J-C, et al. Autoimmune hepatitis with initial presentation as acute liver failure in young children. J Pediatr 1990;116:280-2.
6. Flowers MA, Heathcote J, Wanless IR, Morris S, Reynold WJ, Cameron J, et al. Fulminant hepatitis as a consequence of reactivation of hepatitis B virus inection after discontinuatin of low-dose methotrexate therapy. Ann Intern Med 1990;112:381-2.
7. Saracco G, Macagno S, Rosina F. Serologic markers with fulminant hepatitis in persons positive for hepatitis B surface antigen. A worldwide epidemiological and clinical survey. Ann Intern Med 1988;108:380-3.
8. Trey C, Davidson CS. The management of fulminant hepatic failure. In: Popper H, Schaffner F, editors. Progress in liver failure. New York: Grune and Stratton, 1970;292-8.
9. Gimson AES, O'Grady J, Ede RJ, Portmann B, Williams R, Late onset hepatic failure: clinical, serological and histological features. Hepatology 1986;6:288-94.
10. Khuroo MS, Dar MY, Subacute hepatic failure: experience at Institute of Medical Science, Srinagar. Ind J Gastroenterol 1993;12(Suppl):7-10.
11. Tandon BN. Subacute hepatic failure: definition, nomenclature and criteria for diagnosis. Ind J Gastroenterol 1993;12(suppl): 5-6.
12. O'Grady JG, Schalm SW, Williams R. Acute liver failure: redefining the syndromes. Lancet 1993;352:273-5.
13. Bernuau J. RueffB, Benhamou JP. Fulminant and subfulminant liver failure: definition and causes. Semin Liver Dis 1986;6:97-106.
14. Sherlock S, Dooley J. Diseases of the liver and biliary system. 9th edition. Oxford: Blackwell Scientific Publications, 1993.
15. Riordan SM, Williams R. Treatment of hepatic encephalopathy. N Eng J Med 1997;337:473-8.
16. Khuroo MS, Khuroo N. Hepatitis E: global epidemiology with special reference to impact of the disease in India and the South East of Asia. In: Rizzetto M, Purcell RH, Gerin JL, Verme G, editors. Viral hepatitis and liver disease. Turin: Edizioni Minerva Medica. 1997;601-8.
17. O'Grady JG, Portmann B, Williams R. Fulminant hepatic failure. In: Schiff L, Schiff ER, editors Diseases of the liver. Philadelphia: Lippincott Company 1993;1077-90.
18. Mahler H, Pasi A, Kramer JM, Schulte P, Scoging AE, Bar

W. Krahenbuhl S. Fulminant liver failure in association with the emetic of Bacillus cereus. N Engl J Med 1997;336:1142-8.

19. Bray GP. Liver failure induced by paracetamol. Brit Med J 1993;306:157-8.
20. Vale JA, Proudfoot AT. Paracetamol (acetaminophen) poisoning. Lancet 1995;346:547-52.
21. Zimmerman HJ, Maddrey WC. Acetaminophen (paracetamol) hepatotoxicity with regular intake of alcohol: analysis of instances of therapeutic misadventure. Hepatology 1995;22:588-97.
22. Schiodt FV, Rochling FA, Casey DL, Lee WM. Acetaminophen toxicity in an urban country hospital N Engl J Med 1997;337:1112-7.
23. Khuroo MS, Teli MR, Skidmore S, Sofi MA, Khuroo MI. Incidence and severity of viral hepatitis in pregnancy. Am J Med 1981;70:252-5.
24. Nanda Sk, Yalchinkaya K, Panigrahi AK, Acharya SK, Jameel S, Panda SK. Etiological role of hepatitis E virus in sporadic fulminant hepatitis. J Med Virol 1994;42:133-7.
25. Acharya SK, Dasarathy S, Kumer TL, Sushma S, Prasanna KSU, Tandon A, et al. Fulminant hepatitis in a tropical population: clinical course cause, and early predictors of outcome. Hepatology 1996;23:1448-55.
26. Khuroo MS, Acute livr failure in India. Hepatology 1997-26:244-6.
27. Farci P, Alter H, Shimoda A, Govindarajan S, Cheung L, Melpolder JC, et al. Hepatitis C virus-associated fulminant hepatic failure. N Engl J Med 1997;335:631-4.
28. Lian TJ, Jeffers L, Reddy RK, Silva MO, Cheinguer H, Findor A, et al. Fulminant or subfulminant non-A, non-B viral hepatitis: the role of hepatitis C and E viruses. Gastroenterology 1993;104: 556-62.
29. Takahashi Y, Shimizu M, Aetiology and prognosis of fulminant viral hepatitis in Japan: a multicentric study. J Gastroenterol Hepatol 1991;6:159-64.
30. Wright TL. Etiology of fulminant hepatic failure: is another virus involved? Gastroenterology 1993;104:640-53.
31. Fagan EA. Acute liver failure of unknown pathogenesis: the hidden agenda. Hepatology 1994;19:1307-2.
32. Khuroo MS, Discovery of hepatitis G virus. Ann Saudi Med 1997;17:209-16.
33. Heringlake S. Osterkemp S. Trautwein C, Tillmann HL, Boker K, Muerhoff S, et al. Association between fulminant hepatic failure and a strain of GBV viru C. Lancet 1996;348:1626-9.
34. Ede RJ, Williams R. Hepatic encephalopathy and cerebral edema. Semin Liver Dis 1986;6:107-18.
35. Blei AT, Olafsson S, Webster S, Levy R. Complications of intracranial pressure monitoring in fulminant hepatic failure. Lancet 1993;34:157-8.
36. Pereira SP, Langley PG, Williams . The management of abnormalities of hemostasis in acute liver failure. Semin Liver Dis 1996;16:403-12.
37. Rolando N, Harvey F, Brahm J, Philpott-Howarde J, Alexander G, Gimson A, et al. Prospective study of bacterial infection in acute liver failure: an analysis of 50 patients. Hepatology 1990;11:49-53.
38. Chu CM, Chiu KW, Liaw YF. The prevalence and prognostic significance of spontaneous bacterial peritonitis in severe acute hepatitis with ascites. Hepatology 1992;15:799-803.
39. Rolando N, Philipott-Howard J, Williams R. Bacterial and fungal infections in acute liver failure. Semin Liver Dis 1996;16:389-400.
40. Ellis A. Wendon J. Circulatory, respiratory, cerebral and renal derangements in acute liver failure: pathophysiology and management. Semin Liver Dis 1996;16:379-88.
41. Losser MR, Payen D. Mechanisms of liver damage. Semin Liver Dis 1996;16:357-67.
42. Sinclair SB, Greig PD, Blendis LM, Abecassis M, Robers EA, Philips MJ, et al. Biochemical and clinical response of fulminant viral hepatitis to administration of prostaglandin E; a preliminary report. J Clin Invest 1989;84:1063-9.
43. Sheiner P, Sinclair S, Greig P, Logan A, Blendis LM, Levy G. A randomized control trial of prostaglandin E_1 in treatment of fulminant hepatic failure (abstract). Hepatology 1992;16:88A.
44. Harison PM, Wendon JA, Gimson AES, Alexander GJM, Williams R. Improvement by acetylcysteine of hemodynamics and oxygen transport in fulminant hepatic failure. N Eng J Med 1991;324:1852-7.
45. Kaplan MM, current concepts. Acute fatty liver of pregnancy. N Engl J Med 1985;313:367-70.
46. Sibai BM, Taslimi MM, El-Nazer A, Amon E, Mabie BC, Ryan GM, Meternal-perinatal outcome associated with syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preclampsia - eclampsia. Am J Obstet Gynecol 1986;155:501-9.
47. Knox TA, Olans LB. Liver disease in pregnacy. N Engl J Med 1996;335:569-76.
48. Bhaduri B, Mieli-Vergani G. Fulminant hepatic failure: pediatric aspects. Semin Liver Dis 1996;16:345-55.
49. Khuroo MS, Datta DV. Budd-Chiari syndrome following pregnancy. Report of 16 cases with roentgenologic hemodynamic and histologic studies of the hepatic outflow tract. Am J Med 1980;68:113-21.
50. Vons C, Bourstyn E, Bonnet P, Smadja C, Szekely AM, Franco D. Results of portal systemic shunts in Budd-Chiari syndrom. Ann Surg 1986;203:366-70.
51. Ringe B, Lang H, Oldhafer K-J, Gebel M, Flemming P, Georgii A, et al. Which is he best surgery for Budd-Chiari syndrome: venous decompression or liver transplantation? A single center experience with 50 patietns. Hepatology 1995;21:1337-44.
52. Oches A, Sellinger M, Haag K, Noldge G, Herbst EW, Walter E, Gerok W, et al. Transjugular intrahepatic portosytemic stent-shunt (TIPS) in the treatment of Budd-Chiari syndrome. J Hepatol 993;18:217-25.
53. Cashland TM, Shaw BW Jr., Tape E. The American experience with transplantation for acute liver failure. Semin Liver Dis 1996;16:427-32.
54. Bismuth H, Samuel D, Castaing D, Williams R, Pereira SP. Liver transplantation in Europe for patients with acute liver failure. Semin Liver Dis 1996;16:415-25.
55. Bismuth H, Samuel D Castaing D, Adam R, Saliba F, Johann M, et al. Orthotopic liver transplantation in fulminant and subfulminant hepatitis: the Paul Brousse experience. Ann Surg 1995;222:109-19.
56. Moritz JM, Jarrell BE, Munoz SJ, Maddrey WC. Regeneraton of the native liver after heterotopci liver transplantation for fulminant hepatic failure. Transplantation 1993;55:952-4.
57. Mortiz MJ, Jarrell BE, Armenti V, Radomski J, Carabasi RA, Zeitouni G, et al. Heterotopic liver transplantation for fulmfinant hepatic failure: a bridge to recovery. Transplantation

1990;50:524-6.

58. Gubenatis G, Pichlmayr R, Kemnitz J, Gratz K. Auxiliary partial orthotopic liver transplantatioN (APOLT) for fulminant hepatic failure: first successful case report. World J Surg 1991; 15:660-5.
59. Shaw BH Jr, Cattral M, Langas AN, Heffron TG, Fo IJ. Orthotopic auxiliary liver transplantation: the treatment of choice for acute liver failure? (abstract). Hepatology 1993;18:66A.
60. O'Grady LG, Alexander GJM, Hayllar K, Williams R. Early indicators of prognosis in fulminant hepatic failure. Gastroenterology 1989;97:439-45.
61. Bernuau J, Goudeau A, Poynard T, Dubois F, Lesage G, Yvonnet B, et al. Multivariate analysis of prognostic factors in fulminant hepatitis B. Hepatology 1986;6:648-51.
62. Tygstrup N, Ranek L. Assessment of prognosis in fulminant hepatic failure. Semin Liver Dis 1986;6:129-37.
63. Lee WM, Sorrell MF. Developing a world view toward acute liver failure. Hepatology 1996;24:270-1.
64. Gerlach J. Hybrid Liver support. Int J Artif Organs 1996;19:1-2.
65. O'Grady JG, Gimson AES, O'Brien CJ, Pucknell A, Hughes RD, Williams R. Controlled trials of charcoal hemoperfusion and prognostic factors in fulminant hepatic failure. Gastroenterology 1988;94:1186-92.
66. Hughes RD, Williams R. Use of bioartificial and artifical liver support devices. Semin Liver Dis 1996;165:435-44.
67. Sussman NL, Chong MG, Koussayer T, He D-E, Shang TA, Whisennand HH, et al. Reversal of fulminant hepatic failure using an extracoorporeal liver assist device. Hepatology 1992;16:60-5.
68. Sussman NL, Finegold MJ, Kelly JH. Recorery from syncytial giant-cell hepatitis (SGCH) following treatment with an extracorporeal liver assist device (ELAD) (abstract). Hepatology 1992;16:51A.
69. Moscioni AD, Roy-Chowdhury J, Barbour R, Bown LL, Roy-Chowdhury N, Competiello LS, et al. Human liver cell transplantation: prolonged function in athymic rats. Gastroenterology 1989;96:1546-51.
70. Moscioni AD, Nanney L, Brown L, Barbour R, Demetriou AA. Transplantation of microcarrier-attached human hepatocytes into Gunn rats. Surg Forum 1987;38:385-7.
71. Demetriou AA, Whiting JF, Feldman D, Levenson SM, Roy-Chowdhury N, Mosconi AP, et al. Replacement of liver function in rate by transplantation of microcarrier-attache hepatocytes. Science 1986;233:1190-2.
72. Rozga J, Bellew T, Moscioni AD, Demetriou AA. Transplantation of microencapsulated hepatocytes into analbuminemic rats. Surg Forum 1991;42:419-21.
73. Roy-Chowdhury J, Grossman M, Gupta S, Roy-Chowdhary N, Baker JR, Wilson JM. Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR deficient rabbits. Science 1991;254:1802-5.
74. Grossman M, Wilson JM. Frontiers in gene therapy: LDL receptor replacement for hypercholesterolemia. J Lab CLin Med 1992;"9:457-60.
75. Demetriou AA, Reisner A, Sanchez J, Levenson SM, Moscioni AD, Roy-Chowdhary J. Transplantation of microcarrier-attached hepatocytes into 90% partially hepatectomized rats. Hepatology 1988;8:1006-9.
76. Fair J, Maley W, Stephenson G, Kittur D, Klein C. Extracorproeal procine liver perfusion as a successful bridge to orthotopci liver transplantation (OLT) (abstract). Gastroenterology 1993;104:899A.
77. Chari RS, Collings BH, Magee JC, DiMaio JM, Kirk AD, Harland RC, et al. Brief report: treatment of hepatic failure with ex vivo pig liver perfusion followed by liver transplantation. N Engl J Med 1994;331:234-7.
78. Cramer DV. The use of xenografts for acute hepatic failure. Transplant Proc 1995;27:80-2.

CURRENT STATUS OF MANAGEMENT OF CORONARY ARTERY DISEASE IN DIABETIC PATIENTS

H.S.Rissam MD, DM: S.Kishore, Ashok Sharma, Naresh Trehan

Introduction

Diabetes Mellitus (DM) is a major risk factor for Coronary Artery Disease (CAD). The CAD mortality is three times higher in diabetics (particularly in IDDM) than in non-diabetics . Mortality is further higher in females as compared to males[1] In diabetics there is an interplay of factors like a) Silent Myocardial Ischemia(SMI) - due to which many acute episodes are missed for long b) Cardiac denervation - which interferes with normal rate response causing relative tachycardia thus reducing total diastolic filling time for coronaries and c) Diabetic cardiomyopathy. These factors lead to high morbidity and mortality.[2,3] Micro-albuminuria is an important predictor of CAD in diabetics as the mechanism of escape of albumin through glomerulus is similar to escape of lipoprotein through endothelium into the sub-intimal space which causes accelerated atherosclerosis.[4,5]

Prevalance of Coronary Artery Disease in DM

It is estimated that there are more than 15 million diabetics in India. NIDDM contributes to 95% of all diabetic patients. IDDM increases the risk of death in CAD by 35% as compared to 6% in general population[6] The cardioprotective effect of hormones does not play a significant role in pre-menopausal diabetic women. Framingham study has shown a higher incidence of CAD, Acute Myocardial Infarction (AMI), Angina Pectoris and Sudden Cardiac Death (SCD) in diabetic women over men.[7] GUSTO angiographic trial has shown that there is high frequency of multiple vessel disease 54% vs 40% in diabetics than non-diabetic population and that the diameter of infarct related artery is smaller in diabetics than in non diabetic patients.[8]

Hyperglycemia promotes thrombosis.The responsible mechanisms are :

1) There is altered platelet function and number leading to increased adhesiveness and spontaneous platelets activation and hypercoagulability state.[9,10]
2) Endothelial Dysfunction in Hyperglycemia is due to
    - Low EDRF production
    - Low prostacylin production
    - High free radical formation
    - High Thromboxane A_2 Production
    - High factor V11 and anti-thrombin 111 production[11]
3) High platelet- growth- factor and insulin like growth -factors may induce smooth muscle proliferation (SMC)

CAD in Diabetics - Special Problems

Acute ischemia/Angina : During ischaemia cardiac muscle shifts from aerobic metabolism (Fatty acids utilisation) to anaerobic metabolism (glucose utilisation). Due to insulinopenia, glucose can not enter the myocytes, which causes worsening of ischaemia.

High level of stress hormones increase fatty acids and ketone levels which further impede glucose entry in the myocytes.All the above factors lead to aggravation of ischaemia.[12,13]

Hyperglycemia induces angina in patients with DM by impairing coronary microvascular responses as studied through Coronary Flow Reserve estimations (CFR) by using Doppler Flow Techniques both before and after glucose challenge.[14]

Diabetic patients with unstable angina have increased mortality in first three months as compared to non-diabetics.

Myocardial Infarction : Diabetics with non-q MI need aggressive utilisation of cardiovascular resources like coronary angiography for delineation of coronary artery anatomy as they have higher morbidity and mortality during the first year of the events.Therefore , the culprit lesions need to be identified and dealt with by an appropriate mode of revascularisation.

GUSTO-1 trial reveals the influence of DM on clinical outcome in the thrombolytic era.[15] Diabetes remains an independent predictor of mortality at one month (13%, 10% & 6%)in IDDM, NIDDM and Non-DM respectively. Aggressive insulin therapy is required in AMI patients to prevent myocardial damage and reduce morbidity and mortality. As seen in Swedish study

JK-Practitioner 1999; 6(3): 191-193

From Escorts Heart Institute and Research Centre, New Delhi, India (Rissam, Kishor,Shama, Trehan)

Received March 1999 **Accepted May 1999**

Correspondence to : Dr.H.S.Rissam MD.DM.FCCP.FIMSA, Senior Consultant Cardiologist, Escorts Heart institute and Research Centre, New Delhi.

Diabetic Patients in Acute Myocardial Infarction (DIGAMI), I/V insulin followed by 4 daily s/c injections reduce one- year-mortality to 8.6% (vs 13.5% in those on traditional regimens).[16] The use of sulphonylureas and biguanides is to be avoided due to risk of arrhythmias and lactic acidosis respectively.Beta blockers improve survival after AMI in DM vs Non - DM.[17] Thrombolysis in AMI is usually delayed in diabetics due to missed diagnosis because of either SMI or atypical symptoms.Therefore, patients with AMI must receive thrombolytic therapy whenever they reach hospitals within the "window period".[18] ISIS-2 study has shown a greater reduction of mortality in diabetics who are thrombolysed.[19]

Those patients who continue to show signs of on-going ischaemia, early myocardial revascularization is recommended

Re-Vascularisation in Diabetes

Percutaneous Transluminal Coronary Angioplasty (PTCA): 10-22% of patients undergoing angioplasty are diabetics. Patients in this group are generally post-MI , older, more women, with advanced disease, unstable angina , congestive cardiac failure and they are more likely to have calcified coronaries. In IDDM group 31% of diabetics undergoing PTCA have poor renal functions and low Left Ventricular Ejection Fraction (LVEF).

After PTCA , there is higher incidence of appearance of new narrowings (22% vs 12% in DM vs Non-DM).[20,21] Re-stenosis is major problem after PTCA in diabetic patients. DM leads to endothelial dysfunction and increased platelet - aggregation. Both these factors lead to thrombus formation. Growth factors known to promote restenosis are over expressed in presence of hyperglycemia. Patients with DM exhibit abnormal wound healing which has superficial similarity to the healing process in a vessel after intimal injury in angioplasty.[22-24]

GUSTO angiographic trial has shown that over-all mortality, 30-day and rescue mortality are higher in DM than Non-DM. The "procedure failure" rate is 22% vs 11%.

Other studies like STEIN[25] (1995) and FAXON[26] (1995, 8-year study) have compared PTCA in DM vs Non-DM .They have found higher incidence of death, myocardial infarction, and "need for surgery " two times more in diabetics.

Thus, strict glycemic control may down-regulate the pro-thrombotic and pro-stenotic factors.It is also known that elastic recoil and vasospasm contribute little to in-stent stenosis. It is intimal hyperplasia which is responsible for the lumen loss.[27] Pre-irradiation techniques are seen to decrease the restenosis to 77%. Follow-up studies of Intra Coronary Stents used after angioplasty shall possibly show reduction in the rate of restenosis.

Coronary Artery Bypass graft Surgery (CABG) : Coronary Artery Surgery Study (CASS) showed poor outcome of surgery in diabetics i.e 57% increase in the risk of death as compared to non-diabetics.[28] There is progression of lesions in native arteries and occlusion of grafts. Various trials have shown that CABG is better than PTCA in three vessel disease.[29-31] Important among them is BARI trial (1995, Five-year-outcome). That has shown better results with CABG as compared to PTCA both in terms of mortality (19% vs 35%) and repeat revascularisation (8% vs 62%).[32,33]

Morris et al have shown 5-year survival probability of 0.91 in non-DM and 0.80 in DM (p0.0001)[34] Refinement in surgical techniques and anaesthetics are resulting in better myocardial preservation and enhanced graft patency.More frequent use of IMA grafts has improved surgical outcome. Use of IMA grafts provides survival benefit to both but does not negate the adverse effect of DM on survival as compared to non-diabetics. In diabetics Transmyocardial and Percutaneous Myocardial Laser Revascularisation have offered another treatment option in patients with diffuse disease. Minimally invasive surgical techniques like minithoractomy and Port-access surgery coupled with use of Robotics promise to decrease morbidity and mortality particularly in diabetics with nephropathy and other organ dysfunctions .

Conclusions

1. Asymptomatic diabetic patients need comprehensive investigative work-up for early detection of CAD as they are likely to have silent myocardial ischemia. If non-invasive tests like Treadmill, Stress Thallium are ambiguous or positive, the critical coronary artery lesions must be identified by coronary angiography without delay.
2. Diabetic patients with established CAD (non-Q-MI & Q-MI) must be evaluated with early coronary angiography to identify critical lesions for preventing re-infarction or infarction in other territories by early interventional procedures.
3. Those with acute myocardial infarction must receive aggressive insulin therapy
4. Patients with triple vessel disease do better with CABG than PTCA.

References

1. Jullien J.Diabetic complications. J. Diabetic complications

1997;11:123-30.

2. Almong C , Pik A.Acute myocardial infarction as a complication of Diabetes Mellitus.JAMA 1978;239:2782.
3. Bell DSH: Diabetic Cardiomyopathy.A unique entity or a complication of coronary artery disease ? Diabet.Care 1995;18:708-14.
4. Messent JWC, Eliot TG, Hill RD .Prognostic significance of microalbuminuria in IDDM: a twenty three year follow-up study. Kidney Int. 1992;41:836-39.
5. Jensen T, Stender S, Deckert T.Abnormalities in plasma concentration of lipoproteins and fibrinogenin type1 IDDM patients with increased Urinary albumin excretion. Diabetologia 1988;31:142-45.
6. Aronow WS, Ahn C.Risk factors for new coronary artery events in a large cohort of very eldery patients with and without coronary artery disease . Am J.Cardiol 1996;77:864-6.
7. Garcia MJ, Mc Namara PM, Gordon T. Morbidity and mortality in Diabetics in the Framingham population:sixteen year follow-up study.Diabetes 1974; 23:105-11.
8. Woodfield SL, Lundeergan CF, Reiner JS.Angiographic findings and outcome in diabetic patients treated with thrombolytic therapy for acute myocardial infarction:The GUSTO 1 experience. J Am coll. cardiol 1996; 28:1661-9.
9. Shaw S , Pegrum GD ,Wolf SS. Platelets adhesiveness and diabetes mellitus.J.Clin. Pathol.1967;20:845-7.
10. Mayne EE, Bridges JJ, Weaven JA. Platelets adhesiveness, plasma fibrinogen and Factor-V111 levels in diabetes mellitus.Diabetologia 1970;6:436-40.
11. Catalano DG, Averna M, Notarbartolo A. Thromboxane biosynthysis and platelets functions in Type -2 diabetes mellitus .N Engl J Med 1990;322:1769-74.
12. Hsuch WA, Law RE. Cardiovascular risk continuum implications of Insulin resistence and diabetes.Am J Med 1998; 105:4s-14s.
13. Fava S, Azzopardi J, Agius Muscat H. Outcome of unstable angina in patients with Diabetes mellitus.Diabet Medicine 1997;14:209-13.
14. Lickerman A, Grover McKay M, Dellspergen KE. Hyperglycemia induced angina pectoris in patient with diabetes mellitus.Clin.Cardiol 1997;20:736-7.
15. Mak KH, Moliterno DJ, Granger CB.Influence of DM on clinical outcome in the thrombolytic era of acute myocardial infarction.Gusto-1 investigation.Global utilisation of streptokinase and tissue plasminogen activator for occluded coronary artery. J Am Coll.Cardiol 1997; 30:171-9.
16. Malmberg K, Ryden L, Herlitz J. On behalf of the DIGAMI study group:Randomised trial on insulin glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction(DIGAMI) :effects on one-year mortality. J Am Cardiol 1995; 26:57-65 .
17. Kiekshus J, Gilpin E, Cali G l. Diabetic patients and beta blockers after acute myocardial infarction.Eur.Heart J 1990; 11:43-50.
18. Granger CB, Califf RM, Young SH. Outcome of patients with diabetic mellitus and acute myocardial infarction treated with thrombolytic agents. J Am coll. cardiol 1993; 2:920-25.
19. ISIS-2 Collaborative Group:Randomised trial of 1/V streptokinase, oral Aspirin both or neither among 17817 cases of suspected myocardial infarction. Lancet 1988; 2:349-60.
20. Kip KE, Faxon DP, Detic KM. Coronary angioplasty in diabetic patients. The National Heart Lung and blood Institute percutaneous trans-luminal coronary angioplasty registry. Circulation 1996; 94:1818-25.
21. Stone P, Muller J, Hartwell T. The effect of Diabetes mellitus on prognosis and severe left ventricular function after acute MI:Contribution of both coronary artery disease and left ventricular dysfunction to the adverse prognosis.J Am Coll Cardiol 1989;14:49-57.
22. Simonton CA, Mark DB, Hinohara T. Restenosis following successful coronary angioplasty.:A multivariable analysis of patients, procedures and coronary lesions related risk factors. J Am coll. cardiol 1987 (Abstracts); 9:184A .
23. Hollman J, Badhwar K, Beck GJ. Risk factors for recurrent coronary stenosis following successful coronary angioplasty. Cleve Clin J Med 1898; 56:517-23.
24. Lambert M, Bonan R, Cote G. Multiple coronary angioplasty:a model to discriminate systemic and procedural factors related to restenosis. J Am coll. cardiol 1988; 12:310-14.
25. Stein B, Weintraub WS, Gebhart SP. Influence of diabetes mellitus on early and late outcome after Percutaneous Trans-luminal Coronary Angioplasty. Circulation 1995; 91:979-89.
26. Faxon DP, Kip KE, Currier JW. Diabetics have a significantly poorer eight year outcome after angioplasty. Circulation 1995; 92:1-76.
27. Weintraub WS, Kosinski AS, Brown CL. Can restenosis after coronary angioplasty be predicated from clinical variables? J Am coll. cardiol 1993; 21:6-14.
28. Alderman EL, Corley SD, Fischer LD. Five-year Angiographic follow-up of factors associated with progression of coronary artery disease in the Coronary Artery Surgery Study (CASS). J Am Coll Cardiol 1993; 22:1141-54.
29. Barsness GW, Peterson ED, Ohman EM. Relationship between diabetes mellitus and long term survival after coronary bypass and angioplasty. Circulation 1997; 96:2551-6.
30. Herlitz J, Wognsen GB, Emanuelson H. Mortality and morbidity in diabetic and non diabetic patients during a two year period after coronary artery bypass grafting. Diabetic care 1996; 19: 698 - 703.
31. Weintraub WS, Stein B, Kosinski AS. Outcome of coronary bypass surgery vs coronary angioplasty in diabetic with multi-vessel coronary artery disease. J Am coll. cardiol 1998; 31:10-9.
32. The Bypass Angioplasty Revascularization Investigation (BARI) investigators. Comparison of coronary by pass surgery with angioplasty in patients with multivessel disease.N Engl J Med 1996; 335:217-25.
33. Rozenman Y, Sapozmkou D, Mosseri M. Long term angiographic follow up of Coronary ballon angioplasty in patients with DM. BARI Trial. J Am Coll.Cardiol 1997; 30:1420-25
34. Morris JJ, Smith R, Jones RH. Influence of diabetes and mammary artery grafts on survival after Coronary Bypass. Circulation 1991 (suppl); 84:275-84.

RISK FACTORS AND PREVENTION OF COLORECTAL CARCINOMA

Omar J. Shah M.S., F.I.C.S, F.A.I.S., Manzoor Ahmad Dar M.S., F.R.C.S., Nazir A. Wani M.S., F.R.C.S., F.I.C.S.

Risk for Colorectal Cancer/Prevention

Colorectal cancer is among the commonest visceral malignancies in developed countries. As estimated 1,38,200 cases occured in U.S. in 1995 with 55,300 deaths[1]. This is potentially preventable disease. The marked geographic variation in incidence and the fact that migrants acquire the rate of their adopted country suggest an important environmental component to colorectal cancer risk. If the risk factors are identical one could think of prevention of this diseases. Although dietary factors have received most of the attention, other factors have also been implicated which include calcium, aspirin, obesity, physical exercise and certain medical conditions.

The majority of large bowel malignancies are adenocarcinomas and often develop from premalignant adenoma, the so called adenocarcinoma sequence. Often the tumours are asymptomatic until it reaches an advanced stage accounting for a relatively poor 5 year survival rate of 59.2%[2]. The risk of getting this disease increases with age but the maximum risk increases after the age of 50 yrs[2]. The life time risk of being diagnosed with this malignancy is 6.14%, in men and 5.92% in women[2]. Majority of symptoms include bleeding, anaemia, weight loss, abdominal or pelvic pain, change in bowel habits and due to advanced disease there may be bowel obstruction or perforation. Although barium enema is very helpful technique in diagnosing but it is less sensitive especially in smaller lesions which can be missed. Colonoscopy forms the most sensitive and specific technique for both localizing and taking a biopsy of the lesion so that a histopathologic confirmation is made. Fecal occult blood tests have been widely used especially in mass screening programmes but it is associated with large number of false positives and false negatives.

Colorectal cancer has been the target of a large number of studies in animals and human. The various factors which have been reported to increase or decrease the risk of colorectal cancer are summarised in table I.

Table 1: Risk factors for colorectal cancer

Decrease risk	Increase risk
Probable	
1. Fiber	1. Total fat
2. Vegetables	2. Saturated fat
3. Aspirin/non-steroids	3. Obesity
4. Physical activity	
5. Calcium	
Possible	
1. Vitamin A.C.E.	1. Meats cooked at high temperature
2. Selenium	2. Iron
3. Anticarcinogens	3. Alcohol
4. Folate	

Diet

The fiber hypothesis formulated in early 1960s by Dennis Burkit observed that African natives had low colon cancer rates and high fecal bulk[3]. This observation was presumed to be the consequence of a high fiber diet. There are many mechanisms whereby fiber could inhibit the development of colorectal cancer including effects on fecal weight, transit time, abosorption of bile acids, dilution of colonic contents, production of short chain fatty acids by bacterial fermentation, alteration of luminal pH, inhibition of hydroxylation of bile acids, and regulation of energy intake[4]. Recently two studies supported the beneficial effects of fiber hypothesis. In one study it was estimated that a 43% reduction in risk occured when highest and lowest extremes of risk were compared[5]. In the other study a conclusion was made that in United States there could be a decrease by 31% if the fiber intake from various foods is made to about 13 gm/day which would represent an increase in fiber of 70%[6]. The fiber is a term which refers to a heterogenous group of carbohydrate and carbohydrate like polymers of plant origin. These compounds resist digestion by human hydrolytic enzymes, although digestion by bacterial enzymes may occur.

Vegetables

There have been a number of studies to see the relationship between vegetables and colon cancer and

JK-Practitioner 1999; 6(3): 194-197

From Department of General Surgery SKIMS, Soura, Srinagar, India (Shah, Dar, Prof. Wani)

Received March 1999 Accepted June 1999

Correspondence to : Dr. N.A.Wani, Bypass, Crossing, Hyderpora, Srinagar, Kashmir 190014, India.

the results are remarkably consistent[7]. In particular members of the cruciferous vegetable family including broccoli, cabbage, and brussels sprouts have been repeatedly shown to be protective. May be some chemical compounds in these vegetables inhibit the production of carcinogens. In a study conducted by Thun et al[8] it was shown that vegetables and grains decreased the colon cancer risk by 25% for men in the highest quintile of consumption compared with the lowest and by 38% in women. More than 100 chemical species from plant kingdom have been found to be antimutagenic, anticarcinogenic or antipromotional in their mechanism of inhibition.[9] Examples include thioethers (garlic, onions, leeks), terpenes (citrus fruits), plant phenols (grapes, strawberries, apples) and carotenoids (carrots, yams, watermelon). Other anticarcinogens include isothiocyanates, methylated flavones, coumarins, sterols, selenium, ascorbic acid, tocopherols and carotenoids all of which have action at various points in carcinogenesis.

Vitamins and Trace metals

Although current data does not support the use of antioxidant vitamins for colon cancer prevention but there are reasons to believe that antioxidant vitamins (A,C,E) may be useful chemopreventive agents. It has been seen that these agents by inhibiting free radical reactions, prevent oxidant damage to DNA. Another study conducted by Potter et al[10] showed that population consuming vegetables containing these vitamins are at low risk for development of colon cancer. A study conducted in adenoma patients who were supplemented with vitamins A, C and E showed that cell kinetic abnormalities were normalized by using such vitamins[11]. Conversely there have been trial on polyp patients which showed mixed results[11-15]. Thus at present use of such elements in prevention of colon cancers is not suggested.

Another vitamin which has generated interest is folate. DNA methylation is a major determinant of histone binding, chromosomal structure and gene transcription. In colon cancer DNA hypomethylation is an early step. As folate is a methyl donor, thus folate deficiency may be related to the development of colon cancer. Alternatively folate may promote the synthesis of thymidylate, which may prevent cells from being arrested in the S phase of the cellular growth cycle and erroneously incorporating uridylate into DNA during synthesis[16]. Folate is showing to be a promising agent and is currently included in various polyp prevention trials.

Various trace metals like selenium, zinc, iron and fluoride have been suggested to be important in colon carcinogenesis[17]. Selenium unfortunately can be toxic, has been shown to have a cancer preventive effect. It may alter carcinogen metabolism, affect immune function, protect against oxidant stress, inhibit cell proliferation and impair tumor metabolism. Clark et al have shown that patients with low plasma selenium were at four times the risk for development of adenomas[18]. Iron has been shown to increase the risk of colorectal adenomas possibly by generating free radicals which attack DNA and damage chromosomes[19].

Fish oil and fat

Although no epidemiological studies of fish oil exist but animal studies have shown that experimentally induced colon cancer is enhanced by saturated and Omega-6 polyunsaturated fatty acids and decreased by omega-3 and decosahexanoic acid found in fish oil. Though the effects of fish oil are analogous to administration of aspirin but are broader due to omega-3 fatty acids which inhibits both the cyclo-oxygenase and lipoxgenase pathways. Animal studies have shown a link between fat and colon cancer[20]. Human studies have also shown increased risk of colon cancer in people who consume high fat diet, with saturated fat being more important than unsaturated[21]. The ways by which high fat diet increases the risk of colon cancer seems to be mediated by bile salts. As fat enhances the excretion of cholesterol and bile acids, their degradation products concentration is increased in stool. These have detergent and tissue damaging effects that are associated with increased cell proliferation. Colorectal cancer patients have been found to have differences in metabolizing enzymes that are under genetic control[22]. It may be that people who develop colorectal cancer may have an inherited gene which regulates metabolizing enzymes and exposure to heterocyclic amines in cooked meat and time may be there when such patients may be screened for these genes and dietary changes recommended for those at genetic risk.

Calcium and Alcohol

The mechanism by which calcium binds to fatty and bile acids to form inactive soaps may retard the hyperproliferative stimulus of dietary fat, bile salts and fatty acids which has been well shown in animal studies[23] And even in humans calcium has been shown to offset abnormal cellular proliferation[24,25].

There are various studies which show that there is an association between alcohol mainly beer and large bowel cancer especially rectal cancer[26].

Life style (obesity, exercise, occupation)

It has been indicated that overweight people are at a higher risk of getting colon tumors[27] but it is not certain that the risk relates to obesity, lack of physical exercise[28] or elevated energy intake[29]. Although the mechanism to explain the effect of exercise on colorectal cancer mortality is uncertain, some have noted that the activity stimulates colon peristalsis and decreases random nonpropulsive segmentation activity. Contact time between colonic mucosa and potential carcinogens in the intestinal stream may be decreased by exercise which may decrease the transit time. However some studies suggest no effect but it seems that relationship between exercise, obesity and diet is a complex one. There are reports which suggest that increased rate of colorectal cancer occurs in wood workers, synthetic fiber and asbestos workers[30]; elevated risk has also been seen in people working in petroleum industry, printing machine operators, communication workers and also in those with sedentary jobs[31].

Although in recently conducted studies aspirin and nonsteroidal anti inflammatory agents show great promise as a possible chemopreventive agents for colon cancer[32], but still they are not recommended for general use. As there are several aspirin trials in the field and one should wait for the results before recommending aspirin to the patients.

Medical conditions

There are many conditions which have been seen to be associated with an increased risk of colorectal cancer (table II). Research has shown that careful colonoscopic surveillance can decrease the risk of cancer by 90%[33]. With the availability of genetic test the risk of colorectal cancer can be reduced. First degree relatives with a family history of colorectal cancer have two fold risk of cancer and individuals with adenomatous polyposis coli will develop colorectal cancer which can be prevented by colectomy.

Table 2: Medical conditions that may increase the risk of colorectal cancer

1. History of colorectal adenomas
2. Ulcerative colitis
3. Chron's disease
4. Radiation
5. Family history of colorectal cancer
6. Adenomatous polyposis coli
7. Hereditary nonpolyposis colon cancer (HNPee)
8. Cholecystectomy.

Prevention of colorectal cancer

A. Primary Prevention

There have been various recommendations which have been laid by various cancer groups for the preventaion of this cancer. This includes the guidelines which have been adopted by National Research Council Committee on Diet and Health[34]. The recommendations are as follows.

1. Reduction of total fat intake to 30% or less of calories and reduction of saturated fatty acid intake to less than 10% of calories.
   This view has been taken in accordance with evidences from epidemiologic and laboratory studies which suggest that decrease in total fat intake decreases the risk of colon cancer.

2. Increased intake of combination of vegetables, fruits, especially green and yellow vegetables and citrus fruits. The intake of carbohydrates should be increased to more than 55% of total calories. Although the mechanisms behind are not understood but there is a good evidence of their protective effect.

3. A Balanced food intake and physical activity in order to maintain an appropriate body weight.

4. Maintain adequate calcium intake.

Low or non fat dairy products and dark green vegetables are rich sources of calcium. Amongst the most promising chemoprotective agents under trial in humans and in animals are aspirin and the nonsteroidal anti inflammatory agents, but until more is known about the risks and benefits of these compounds their use is not yet, recommended for general public.

B. Secondary Prevention

This part of prevention aims at screening. American cancer society recommends digital examination, sigmoidoscopy and stool occult blood tests starting at age of 50 years. Despite good reports about efficiency of controlled trial of Hemocult[35], many continue to doubt its worth. There are many false positives and false negatives with this test, and it seems that this test has less important role in screening practice. One of the best screening modalities is colonoscopy, but it has its problems like being too expensive and cumbersome to be endorsed widely as a modality in asymptomatic average risk individuals. Perhaps once or twice a lifetime, screening of entire colon with colonoscopy or barium enema is a more practical approach[36]. At present it seems that a programme of screening sigmoidoscopy should work. This can be done every 5 to 10 years[32]. Nurses have been shown to perform these screening sigmoidoscopies as accurately and safely as by experienced gastroenterologists[38].

As the research on colorectal cancer is going fast, till then it seems logic that programme of life style modification and surveillance would decrease the incidence and mortality from this dreaded disease.

References:

1. Wingo P, Tong T, Bolden S. Cancer statistic 1995, CA 1995; 45:8-30.
2. Reis LAG, Millerr BA, Hankey BF et al. SEER cancer statistics review 1973-1991. Tables and graphs, National Cancer Institute. NIH Pub: No. 94-2789 Bethersda, MD, 1994.
3. Burkitt DR. Fiber in the etiology of colorectal cancr. IUn Winawers, Schottenfeld D, Sherlock Peds. colorectal cancer, prevetion, epidemiology and screening, New York; Raven Press, 1980; 13-19.
4. Jacobs LR. Fiber and colon cancer. Gastroenterol Clin North Am 1988; 17:747-760.
5. Trock B, Lanz E, Greenwall P. Dietary fiber, vegetables, and colon cancer: critical review and meta analysis of the epidemiologic evidence. J. Nalt Cancer Inst. 1990; 82: 650-661.
6. Howe GR, Benito E, Casteleto et al. Dietary intake of fiber and decreased risk oof cancer of the colon and rectum: evidence from the combined analysis of 13 case control studies. J. Nalt Cancer Inst 1992;84:1887-1896.
7. Poller JD. Vegetables, dietary fiber and cancer. J. Nutr 1988: 118: 1591—1592.
8. Thun MJ Calle EE, Namboodiri MM et al. Risk factors for total colon cancer in a large protective study. J. Natl cancer Inst. 1992; 84:1491-1500.
9. Wargovich MJ: New dietary anticarcinogens and prevention of gastrointestinal Cancr. Dis Colon Rectum 1988;31:72-75.
10. Potter JD, Slattery ML, Bostick RM et al. Colon cancer, a review of the epidemiology. Epidemiol Rev. 1993;15:499-545.
11. Paganelli GM, Biasco G, Brandi G et al. Effrect of Vitamin A. C and E supplementation on rectal, cell proliferation in patients with colorectal adenomas. J. Natl Cancer Inst. 1992;84:47-51.
12. Decosse JJ, Miller HH, Lesser ML. Effect of wheat fiber and vitamins C and E on rectal polyps in patients with familial adenomatous polyposis. J. Natl cancer Inst: 1989;81:1290-1297.
13. Bussey H, Decosse J, Dechner E. A randomized trial of ascorbic acid in polyposis coli. Cancer 1982;50:1435-1439.
14. Mcknown EG, Holloway C, Jazmaji V et al. A randomized trial fo vitamins C and E in the prevention of recurrence of colorectal polyps. Cancer Res: 1988; 48:4701-470.
15. Greenberg ER, Baron JA, Tosteson TD et al. A clinical trial of antioxidant vitamins to prevent colorectaladenoma. Polyp prevention study group. N. Engl. J. Med. 1994; 331:141-147.
16. Eto I, Krumdieck CL. Role of vitamin B12 and folate deficiencies in carcinogenesis. Adv exp Biol Med. 1986;206: 313-330.
17. Nelson PL. Dietary minerals and colon carcinogenesis. Anti Cancer Res. 1987;7:259-270.
18. Clark LC, Hixon LJ, Combs GFJ et al. Plasma selenium concentration predicts the prevalence of colorecctal adenomatous polyps. Cancer Epidemiol Biomarkers Prev. 1993;2:41-46.
19. Nelson PL. Dietary minerals and colon carcinogenesis. Anticancer Res: 1987;7:259-270.
20. Reddy BS. Amount and typ of Dietary fat and colon cancer animal model studies. Prog Clin Biol Res 1986;222: 295-309.
21. Willett W. the search for the cause of breast and colon cancer. Nature 1989;338:389-394.
22. Kadulbar FF, Butler NM, Kaderlik KR et al. Polymorphism for aromatic amine metabolism in humans, relevance for human carcinogenesis. Environ Health Persp. 1992;98:68-74.
23. Wargovich MJ. Calcium and colon cancer. J. Am Coll Nutr. 1988;7:2295-2300.
24. Rozen P, Fireman Z, Fine N et al. Oral calcium suppresses increased rectal epithelial proliferation of persons at risk of colorectal cancer. Gut 1989;30:650-655.
25. Lipkin M, Newmark H. Effect of added calcium on colonic epithelial cell proliferation in subjects at high risk for familial colon cancer N. Engl. J.Med. 1985;313:1381-1384.
26. Klastsky AL. Armstrong MA, Friedman GD the relation of alocholi beverage use to colon and rectal cancer. Am J. Epidemiol 1988; 128: 1007-1015.
27. Allbanes D. Caloric intake, body weight and cancer. A review: Nutr cancer 1987;9:199-127.
28. Slattery ML, Schumacher C, Smith KR et al. Physical activity, diet, and risk of colon cancer in Utah. Am. J Epidemoil 1988;1228:9898-9899.
29. Lyon JL, Mdahoney AW, West DW. Energy intake: its relationship to colon cancer risk JNCI 1987;78:853-861.
30. Berg JW Howell MA. Occupation and Bowel cancer. J Toxicol Environ Health 1975;1:75-89.
31. Brownson RC, Zahn SH, Change JC. Occupational risk of colon cancer: an analysis by anatomic site. Am J. Epidemiol 1989;130:675-687.
32. Greenberg ER, Baron JA. Prospects for preventing colorectal cancer death J.Natl Cancer Inst. 1993;85:1182-1184.
33. Winawer SJ, Zamber AG, Ho MN. Prevention of colorectal cancer by colonoscopies polypectomy. N.Engl. J. Med. 1993;329:1977-7181.
34. Committee on Diet and Health, National Research Council. Diet and Health, Implication for reducing chronic disease risk. Washington DC: National Academy Press 1989.
35. Mandel JS, Bond JH, Church TR. Reducing mortality from colorectal cancer by screening for fecal occult blood. N. Engl. J. Med. 1993;328:1365-1371.
36. Lieberman DA, Smith FW, Screening for colon malignancy with colonoscopy, Am. J. Gastrooenterol 1991;86:946-951.
37. Atkin WS, Cuzick J, Northover JMA, et al. Prevention of colorectal cancer by once only sigmoidoscopy Lancet 1993; 241;736-749.
38. Maule WF screening for colorectal cancer by nurse endoscopists, N.Engl J. Med. 1994'330:183-187.

SINUS HISTIOCYTOSIS WITH MASSIVE LYMPHADENOPATHY

Gangadharan, V.P., M.D., D.M.; Prakash N.P. M.D.; Jayasree K. M.D.; Seethalaxmi N.V. M.B.B.S.;
Ramadas K. M.D.; Elizabath K.A. M.D.; Nileena Nayak. M.D.

Abstract: *Sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman disease) is a pseudolymphomatous disorder presenting with massive lymphadenopathy and constitutional symptoms like fever and anaemia. Extranodal involvement is being increasingly recognised. We present five cases with diverse clinical picture, including extranodal presentations.*

Key words: *Sinus histiocytosis with massive lymphadenopathy, Rosai Dorfman disease.*

JK-Practitioner 1999; 6(3): 198-200

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML) or rosai-Dorfman disease is a clinical syndrome characterised by painless lymphadenopathy associated with fever, anaemia, neukocytosis, elevated erythrocyte sedimentation rate and polyclonal hypergammaglobulinemia[1,2]. Majority of SHML patients have a benign course and about 10% have clinically significant immunological abnormalities with high fatality rate[3,4].

Although majority of these cases present with nodal disease, 30% can have extranodal manifestation[5]. We describe 5 cases presenting with varying clinical picture including skin involvement, pathological fracture of bone and vertebral involvement. Response to steroids, cytotoxic agents and radiation therapy are transient.

Discussion

Sinus histocytosis with massive lymphadenopathy (SHML) was first described by Rosai and Dorfman in 1969. It classically presents in the first or second decade with massive bilateral painless cervical lymphadenopathy. Approximately 30% have extranodal manifestations. Common extranodal sites involved are skin[6], eyes[7], central nervous system[8,9,10], upper aero digestive tract[11] and bone[12]. Rare extranodal presentations reported include colonic perforation[13] erythroderma and hair loss[14] and a variety of head and neck sites[15].

The aetiology of the disease still remains unknown. In 1972 Rosai and Dorfman suggested that SHML might be aberrant reaction to an infectious process in the context of an altered immune status. Foucar et al demonstrated immune dysfunction in 10% of SHML patients which include hematologic auto antibodies, glomerulo nephritis, Wiskott Aldrich syndrome, joint diseases etc[16].

Histopathologically, SHML is characterised by pericapsular fibrosis and widening of nodal sinuses distended with large histiocytes having abundant clear cytoplasm showing prominent emperipolesis or lymphophagocytosis. Compressed residual intersinusoidal tisuse show paucity or absence of germinal centres and marked proliferation of plasma cells.

Immunohistochemically, the histiocytosis in SHML are positive for S-100 protein, alpha-I antichymotrypsin (ACT) and cathepsins. Thus the taxonomy of these histiocytes is difficult to define, as they share properties of dendritic cells as well as those of ordinary hitiocytes.

SHML needs to be differentiated from Malignant histiocytosis having a rapidly fatal clinical course and the haemophagocytic syndromes. Histiocytes in Malignant histiocytosis show malignant features and are monoclonal. SHML has been shown to be a polyclonal histiocytic disorder. In infection associated haemophagocytic syndromes there is prominent crythrophagocytosis in bone marrow, spleen and lymphnodes in contrast to the lymphophagocytosis in SHML. SHML characteristically spares the spleen and bone marrow.

Majority of SHML patients have a benign course. Spontaneous remission occur frequently. Rare, but serious sequele are retropharyngeal involvement with respiratory embarassment and epidural involvement with spinal cord compression[18]. Patients with immunologic dysfunction and extra nodal disease have worse prognosis with significant mortality rate.

A case of SHML presenting with multiple skin and

From the Departments of Medical Oncology (Prof. Gangadaran, Prakash, Seethalaxmi), **Pathology** (Elizabath, Nayak, Jayasree) **and Radiotherapy** (Ramdas) **Regional Cancer Centre Thiruvananthapuram, India**

Received May 1998 Accepted June 1999

Correspondence to : Prof. Gangadharan V.P., Head, Division of Medical Oncology, Regional Cancer Centre, Thiruvananthapuram-695011, India, Phone-91-471-446844, Fax: 91-471-447454

Clinical Profile

Case No.	1	2	3	4	5
Age (in years)	15	30	7	40	16
Sex	Female	Male	Male	Female	Female
Fever	+	+	+	+	+
Pallor	+	—	+	—	+
Lymphadenopathy	generalised	cervical	generalised	cervical	cervical
Hepatomegaly	+	+	+	—	—
Splenomegaly	+	—	+	—	—
Extra Nodal involvement	skin nodule	—	D$_1$ vertebra collapse	pathological fracture of radius	—
Hb (gm%)	9	11	7	12.6	8
ESR mm/1hr	87	125	105	160	115
Serum proteins Total (gm%)	7.2	8.5	6.8	8.1	9.4
Albunim : Globulin	3.35 : 3.85	2.7 : 5.8	3 : 3.38	3.9 : 4.2	3 : 6.4
Serum Electrophoresis	polyclonal	polyclonal	polyclonal	polyclonal	polyclonal
Chest X-ray	Bilateral paratracheal nodes+	Superior mediastinal nodes+	right para tracheal nodes	normal	superior paratracheal nodes
Cervical lymphnode biospy	SHML	SHML	SHML	SHML	SHML
Bone marrow biopsy	Normal	Normal	Normal	Normal	Normal
S-100 protein	+	+	+	+	+
Blood, urine & throat culture	Sterile	Sterile	Sterile	Sterile	Sterile
Treatment	Steroid → COP* → XRT**	Steroid → COP	Steroid → COP → XRT	Steroid	Steroid
Course of diasese	Progressive disease and death due to infection at 23 months follow up	Progressive disease and death due to infection at 18 months	Alive follow up 44 months	Alive follow up 26 months follow up	Alive follow up 12 months

* COP → Cyclophosphamide, Vincristine, Prednisolone
** XRT → External radiotherapy

subcutaneous nodules and multiple osteolytic lesions has also been reported[19]. SHML has been reported in association with non Hodgkin's lymphoma and nodular lymphocyte predominant Hodgkin's disease[20,21].

SHML of soft tissues has been reported recently with a tendency for recurrence obviating the need for an aggressive surgical approach[22]. Soft tissue lesions can involve the extremities, trunk, head and neck and the retroperitoneum. SHML in extranodal sites show more subtle histologic features than the nodal counterparts with less conspicuous lymphophagocytosis and pronounced fibrosis, thus mimicking fibrohistiocytic and inflammatory lesions[23]. S-100 positively will help in confirming the diagnosis[24].

References:

1. Rosai J, Dorfman R.F., Sinus Histiocytosis with massive lymphadenopathy. Arch Pathol, 1969;87:63-70.
2. Rosai J, Dorfman R.F., Sinus Histiocytosis with massive lymphadenopathy. A pseudolymphomatous benign disorder. Cancer 1972;30:1174-1188.
3. Lampert F, Lennert K. Sinus Histiocytosis with massive lymphadenopathy. A pseudolymphomatous benign disorder. Cancer, 1972:30-1174-1188.
4. Dearth J, Hunter D, Kelly D, Crist W. Sinus Histiocytosis with massive lymphadenopathy. CA: 1980;30:55.
5. Sanchez. R.Rosai J., Dorfman R.F., Sinus histiocytosis with

massive lympadenopathy. An analysis of 113 cases, with special emphasis on its extranodal manifestations Abstr. Lab invest; 1977;36:21-22.

6. Thawerani H, Sanchez R.L., Rosai J, Dorfman R.F. The cutaneous manifestations of sinus histiocytosis with massive lymphadenopathy. Arch Dermatol 1978;114:1991-1997.
7. Foucar E, Rosai J., Dorfman R.F. The ophthalmologic manifestations of sinus histiocytosis with massive lymphadenopathy. Am. J. Opthamol; 1979;87:354-367.
8. Foucar E, Rosai J., Dorfman R.F., Brynes R.K. The neurologic manifestation of sinus histiocytosis with massive lymphadenopathy. Neurology; 1982;32:365371.
9. Clark W.C., Berry A.D., Extranodal SHML; isolated CNS involvement mimicking meningioma. South Med. J.: 1996;89(6): 621-623.
10. Katz D.S., Poe L.B, Corona R.J. (Jr.), SHML. A case of simultaneous upper repriatory tract and CNS disease without lymphadenopathy. Am. J. Neuro Radiol 1993;14(1): 219-222.
11. Foucar E, Rosai J., Dorfman R.F., Sinus histiocytosis with massive lymphadenopathy: Ear, nose and throat manifestions. Arch Oto laryngol; 1978;104:687-693.
12. Walker P.D., Rosai J and Dorfman R.F. The osseous manifestations of sinus Histiocytosis with massive lymphadenopathy. Am. J. Clin Pathol. 1981;75:131-139.
13. Amraoui M, Bougtab A.Alami H, et al. An exceptional case of colic perforations. Sinus haemophagocyte histocytosis. J. Chir, 1994;131(3): 158-159.
14. Tsukahara T, Horiuchi Y, Ohykawa T, et al. M., J. Dermatol; 1993; 20(1):49-55.
15. Wenig B.M. Abbondanzo S.I., Childers E.L., et al. Hum Pathol. 1993;24(5): 483-492.
16. Foucar E., Rosai J, Dorfman R.F., Sinus histiocytosis with massive lymphadenopathy. AN. analysis of 14 deaths occuring in a patient registry. Cancer 1984;54: 1834-1840.
17. Hags J.A., Helmig MSE, Preschtel K. Sinus Histiocytosis with massive lymphadenopathy and paraparesis remission with chemotherapy. A case report. Cander 1978;42:77.
18. Foucr E., Rosai J and Dorfman R.F. Immunological abnormalities and their significance in the sinus Histiocytosis with massive lymphadenoapthy. Am. J. Cli. Pathol. 1984;82:515- 525.
19. Naresh K.N. Mukherje G., Rama Rao C, et al. Extranodal sinus histiocytosis with massive lymphadenopathy - A Case report. Indian Journal of Cancer 1992;29:226-229.
20. Mohadjer C, Sommer K, Schwieder G, Weerda H. SHML in association with a B cell lymphoma of high grade malignancy. Oto Rhino Laryngol: Nov. 1994;4(2):97-100.
21. Maia D.M., Dorfman R.F., Focal changes of SHML associated with nodular lymphocyte predominant Hodgkins disease. Human Pathology 1995;26(12):1378-1382.
22. Levine E.A., Landry M.M., Rosai Dorfman disease of soft tissue. Surgery 1994;115(5): 650-652.
23. Montgomery E.A., Meis J.M. Frizzera G., Rosai Dorfman disease of soft tissue. Am. J. Surg. Pathol. 1992;16(2):122-129.
24. Meittinen M, Paljakka P, Hareri P, Saxen E. Sinus Histiocytosis with massive lymphadenopathy. A nodel and extranodal proliferation of S-100 potein positive Histiocytes. Am. J. Clin Path, 1987;88:270.

DECLARATION UNDER SECTION 5 OF THE PRESS AND REGISTRATION BOOKS ACT OF 1967 AS AMENDED FROM - (SEE RULE I)

1. Title - **JK - PRACTITIONER**
2. Place of publication - Srinagar
3. Periodicity of publication - Quarterly
4. Publisher's name - Dr. G. M. Malik
   Whether Citizen of India - Yes
   Address: Jhelum Market, Batamaloo, Srinagar - 190 010, Kashmir (India)
6. Citizen of India - Yes
   Address: Jhelum Market, Batamaloo, Srinagar - 190 010, Kashmir (India)
7. Particulars of other individuals who are owners/shareholders of Newspaper.

I Dr. G. M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

sd/-
Dr. G. M. Malik

ENDOPYELOTOMY VERSUS CONVENTIONAL PYELOPLASTY IN P.U.J. OBSTRUCTION

H.S.Bhatyal M.S., M.Ch.; Rakesh Sharma D.H., H.M.,M.S.

Abstract: This study has been carried out on 25 patients each of endopyelotomy and open conventional pyeloplasty. The age 18-66 years, mean 37.8 years, male 21 and female 04 and 22-52 years, mean 33.8 years, male 23 and female 02 years were in endopyelotomy group and open pyeloplasty group respectively. Prior to operation all patients were investigated by routine blood tests and renal function tests. I.V.U. was mandatory in all cases. Renogram was done where kidney was not visualized on I.V.P. The results were compared in each group in the form of blood loss, post-operative recovery complications, hospitalisation period, days to return to work and over all success rate. It was seen that endopyelotomy group had advantage in all above variables as compared to open pyeloplasty except success rate was 72% in endopyelotomy and 96% in open conventional pyeloplasty.

Key words: Hydronephrosis, Pyeloplasty, Endopyelotomy.

JK-Practioner 1999; 6(3): 201-203

Introduction:

Hydronephrosis because of pelvic ureteric junction (P.U.J.) obstruction is an important urological entity which for long has puzzled the urological science. It may occur at different ages. The pathophysiology has not been vividly clarified and at the same time spontaneous course of disease is unknown[1].

Surgeons for long with their untiring efforts have established various surgical procedures to achieve the best reconstructive results and the relative merits of each technique are espoused and each has its strong advocates.

Hydronephrosis has been traditionally repaired surgically via open pyeloplasty with success rare of 72-98%[2-4].

The basic aim of all surgical procedures is to relieve symptoms, preserve and improve renal function, decrease complications and lower morbidity and mortality.

To achieve all these, endoscopy has almost revolutionised the management of urological problems. The procedure of endoscopy correction of P.U.J. obstruction is known as pyelysis or endopyelotomy and various authors have reported low complications, less blood loss, less operative time, early recovery and less analgesic requirement and over all success rate of 80-85% when compared to open pyeloplasty where the succes rate has been claimed as 90%[5].

Material and Methods:

This study has been carried out on 50 cases of hydronephrosis because of primary/secondary P.U.J. obstruction. Primary P.U.J. obstruction was found in 39 patients and secondary in 11 patients. Out of the 50 cases (admitted in Army Hospital, Delhi Cantt. between July 1990 to June 1992) 25 were managed by conventional open surgery and other 25 were managed by percutaneous surgery i.e. endopyelotomy. Prior to operation the patients were evaluated by a standard investigation protocol consisting of routine haemogram and renal function test. U.S.G., I.V.U. and renogram in case of non-visuallized kidneys on I.V.U.

Analysis of results in form of success rate, operation time, analgesic requirement, post-operative complication, hospital stay, time taken to return to work in endopyelotomy and open pyeloplasty group were studied and compared with each other.

Results & Observations:

Endopyelotomy

Out of 25 cases of endopyelotomy, 21 were males and 04 females. Their age ranged from 18 years to 66 years and mean age was 37.8 years. The youngest was 18 years and oldest was 66 years.

Anaesthesia: Twenty-two patients were given general anaesthesia and 03 patients were given spinal anaesthesia.

Success Rate: Was defined as removal of P.U.J. obstruction as seen by post-operative renogram/I.V.U. done after six weeks at the time of removal of stent and repeat renogram/I.V.U. done after 03 months. In present series, success rate was 72%.

From the Department of Surgery, Army Research & Referal, Hospital Delhi Cantt. (Bhatyal, Sharma)

Received December 1998 Accepted March 1999

Correspondence to : Dr. (Sqn-Ldr.) Rakesh Sharma, 21, Link Road, Jammu - 180001.

Blood Loss: All the patients experienced small amount of blood loss related to tract dilation and nephroscope manipulation. However, four cases had significant blood loss to cause obstruction of the operative field. In all cases bleeding was temponaded by working sheath. The mean blood loss in endopyelotomy group was 81 c.c.

Operative Time: It was defined as the interval between the time of puncture of pelvicalyceal system to the time of incision in P.U.J. area and placement of nephrostomy. It varied from 60 mins. to 75 mins. and mean operating time was 62.4 mins.

Post-operative Recovery: Most of the patients were put on oral fluids on day 1 after 8 to 12 hours of operation. Seventeen patients i.e. 94.4% were ambulatory on the same day and one patient i.e. 5.5% became ambulant on Ist post-operative day .

Complications: All patients were folllowed upto minimum of 3 months to maximum of 1 year. Most of the patients had minor complications, like fever in 12 patients (66.6%), haematuria 02 patients (11.1%) U.T.I. 03 patients (16.6%), urinary leak 05 patients (27.7%).

Hospitalisation: It was defined as the days of hospital stay from the date of admssion to the date of discharge. The mean hospitalisation period in our study was 7 days.

Days to Return to work: This was defined as the number of days after the discharge from hospital to return to work. Majority of the patients in our study returned to work between 12 to 20 days. The mean days of return to work was 15 days.

Conventional open surgery

Twenty-five patients underwent open surgical procedures. The age ranged between 22 to 52 years and the mean age was 333 years. The youngest patient was 22 years and the odest 52 years. There was 23 males and 02 females.

Anaesthesia: All the operations were performed under general anaesthesia.

Success Rate: Success was judged by the free-flow of dye and decrease in calyceal appearance after doing the I.V.U. after three months and one year. In our series, success rate was 96%.

Blood loss: An average of 200 ml of blood loss was seen and the range was between 150 to 300 c.c.

Operating Tme: The mean operating time was 84 minutes.

Post-operative recovery: Fourteen patients i.e 56% were given oral fluids after first 24 hours, six were given on the post-operative evening and five patients (20%) were given oral fluids on 2nd post-operative day depending on return of bowel sound (table V).

Complications: Nine patients (36%) had fever more than 38°C for more than 3 days. Four cases developed U.T.I. as documented by urine culture. Three patients (21%) had haemeturia. Three patients (12%) developed wound infection. Two patients developed urinary leakage for more than five days which subsequently stopped.

Hospitalisation period: The mean period was 14 days.

Days to return to work: The convalescence period at home in open surgical procedures was between 30 to 50 days. The mean lays of return to work was 45 days.

Discussion:

The main aim of this study was to compare the results of two procedures done for hydronephrosis i.e., open pyeloplasty and endopyelotomy.

In open group out of 25 patients, 19 patients underwent Adernson-Hynes operation. Two patients each were subjected to foly-plasty and spiral flap technique. Only one patient was taken up for Davy's procedure.

Post-operative follow-up was done by doing renogram after six weeks and I.V.U. after three months. Delayed or non—excretion of contrast on I.V.U. was considered as failure. Authors like Eyvind Underbjerg Poulsen et al., however, suggest that renogram should be performed after six months and I.V.U. after 1 year because they have shown that the amelioration in renal function occur within first twelve months post-operatively[1].

The other 25 patients underwent endopyelotomy. Single stage procedure was done in 21 patients and in two stages in four cases[1].

Failure rate was high in endopyelotomy group in our series i.e. 28% (7 out o 25). Failure rate was high in first 10 cases i.e. 50%, but as we gained experience, the failure rate dropped to 13.3%.

J.W.I. Ramsey et al. reported a success rate of 64% in series of 28 cases of Martellli, P.Buli achieved success rate of 77.3%, Gary S. Karlin and A.D. Smith reported a success rate of 88.8%[6]. Van Caugh reported success rate of 85.1%[7].

Operating Time: Gary S. Karlin et al. (1988) reported mean operating time as 75 minutes in pyeloplasty group and 51 minutes in endopyelotomy group. In the present series it was 84 minutes in open procedure and 62.4 minutes for endopyelotomy.

Blood loss: Gary et al. reported on average loss of 85 c.c. in series of 56 patients in endopyelotomy group and 115 ml. loss in open pyeloplasty group. In our series it was 81 c.c. and 200 c.c. respectivly.

Complications: In William seires of 190 patients who underwent pyeloplasty, eight patients (4.21%) had persistent urinary drainage. In two patients it closed spontaneously and in two required retrograde catheterization and there were re-explored. Johnston and Associates in a review of 219 patients had four cases (1.82%) of persistent P.U.J. obstruction[2], further occasional complications of pyeloplasty include stenosis, ureteral kinking, infection and haematuria[8,9].

However, failure to achieve desired results has been the more common complication of endopyelotomy. In Badlani and Association series, 7 out of 64 (10.9%) were considered failure. In a series of 28 patients of Ramsey and Associates, there were five failed pyelolysis[9].

In the present series, fever and urinary leak for more than 7 days were seen in 12 and 05 patients constituting 66.6% and 27.3% of the complications, other complications in endopyelotomy group was U.T.I. 16.6% haemeturia 11.1%, whereas in open group fever was commonest complication in 36%, U.T.I. in 16%, haemeturia in 12% and wound infection in 12%.

Hospitalisation Period: Gary S. Karlin and Associates have reported hospitalisation period of 6.2 and 10 days respectively. In present series, it was 07 and 14 days.

Days to return to work: Again in Gary S. Karlin series, it was 19.8 days in endopyelotomy group and 45 days in open group. In our series, it was 15 and 45 days respectively.

References:

1. Ejvind Underbjerg Poulsen et al.: The functional outcome of Anderson-Hynes Pyeloplasty for Hydronephrosis. Scand. Journal Urol. Nephrol., 1987;21:213-217.
2. Johnston J.H., Evans J.P., Glossberg K.J. and Sehaphiro S.R.: Pelvic Hydronephrosis in children: A review of 219 personal cases. Journal of Urol., 1997; 117:97.
3. Hendren W.H., Randhakrishanan J. and Middleton A.W. Junior: Paediatric Pyeloplasty. Journal of Paed. Surgery, 1980;15:133.
4. Persky L., Krause J.R. an Boltuch R.L.: Initial complication and late results in dismembered pyeloplasty.Journal of Urol., 1977;118: 166,162.
5. Gary S.Karlin, Gopal H. Badlani and Arthur D. Smith: Endopyelotomy vs. OPen Pyeloplasty: Comparison in 88 patients. Journal of Urology, 1988;140:476-478.
6. Gary S.Karlin et al.: Endopyelotomy. UroClinic of North America, 1988; 15(3): 493-443.
7. Van Caugh P.J. et al.: Endopyelotomy, percutaneous treatment of P.U.J. (abstract). Proceeding of the 5th World Congress on Endo-urology and ESWL, Egypt, Page 120.
8. Jettry N. Weiss, Gopal H. Badlani and A.D. Smith: Endopyelotomy vs. Open Pyeloplasty: Comparison in 88 patients. Journal of Uroollogy, 1988; 140, 476-478.

With Best Compliments From

SUPREME SYNDICATE

Complete Hospital and Laboratory Furnishers and
Pharmaceutical Distributors

267, NURSING GARH, SRINAGAR-190 001 (KASHMIR) PHONES : 471528, 478712; FAX : 0194-430645

AUTHORISED STOCKISTS FOR:

CHEMICALS:
E.Merck (I) Ltd.
B.D.H. Chemicls
S.D.Fine Chem. Ltd.
Hi-Media Laboratories

GLASS WARE:
Durani (German) Glass Ware
Blue Star Glass Slides & Cover Slips

EQUIPMENTS:
Getner Microscopes
Suvira Audio Visual Equipments
Sipcon Microtones/Tissue Processors
Jindal Lab. Equipments

ROLE OF RADIO-IMAGING IN MANAGEMENT OF "SURGICAL ASCARIASIS"

Ishtiyak A. Mir M.S.; N.A.Wani M.S.; O.J. Shah M.S; Rehha Patnaik M.S; Khalida Saleem M.S.

Abstract: *The study was conducted on 120 patients admitted with acute and or subacute intestinal obstruction due to ascaris lumbricoides. Plain radiography and ultrasonography of the abdomen was done in all the patients. Contrast study using water soluble media was done in selected patients only. Serial radiological examinations were done to pick up surgical complications caused by ascariasis well in time and also to enable use to continue conservative management with more conviction and confidence. Plain radiography of the abdomen showed gaseous distension of bowel in 76.67%, air fluid level in 53.33%, worm masses in 33.33% of the patients. Contrast study done in 35 patients showed worm masses in 71.42% of the patients. Ultrasonography revealed worm masses in intestines in 23.33%, free fluid in 7.50%, freely moving worms in intestinal lumen in 6.67%, worms in hepatobiliary system in 8.34%, and atonic fluid filled bowel in 13.13% of the patients. Only 10.10% of the patients underwent surgery and 90.00% were managed conservatively.*

Key words: Ascariasis,

JK-Practitioner 1999; 6(3): 204-206

Introduction

History of ascaris lumbricoides is known to stretch back to 35 centuries, discovered in Eber's Papyrus in 1550 B.C. Even at the turn of the century with advanced medicines it still continues to cause symptoms illness, and even death-Bean (1965)[1]. The principal surgical complications occur because of obstruction and perforation of intestinal wall or by obstruction of biliary and pancreatic duct. Desa (1966)[2]. The various criteria for surgical intervention in surgical ascariasis are persistence of mass at the same site, fixity of mass for more than 36 hours, persisting abdominal pain and tender mass, rising pulse rate in absence of any mass and toxaemia out of proportion to the severity of obstruction. Since there is no specific method for the diagnosis of surgical ascariasis controversy still exists regarding the modality of treatment. Radio-imaging techniques were used in the present study with an idea to subject least number of patients to surgery. Repetitive radiological examination helps to pick up surgical complications well in time and define the modality of treatment.

Material and Methods

The study was conducted on 120 patients in paediatric age group over a period of three years, in the department of Paediatric Surgery and Radio-daignosis, SKIMS, Srinagar, Kashmir, India. A detailed clinical evaluation was done in all the patients. Passing of adult worms in vomitus and/or per rectum was present in all at some time of illness. The stool samples of all the patients were positive for ova of ascaris lumbricoides. Total leucocytic count, differential leucocytic count, serum bilirubin and serum amylase were done in all patients.

Radio-Imaging

Plain radiographs of abdomen standing and lying down were performed in all the patients. Follow up radiographs of abdomen were performed to see the effect of conservative line of treatment, such as volvulus, intussusception and visceral perforation. Contrast studies of the gut were conducted in patients who were responding to conservative treatment, had no signs of visceral perforation clinically and radiologically. Water soluble contrast media (meglumine-iothalmate 60%) was used. All these patients were well hydrated and were kept on intravenous fluids throughout the study. Contrast media was given through the nasogastric tube. Films were taken at 2,4,6,12 and 24 hrs duration.

Patients were subjected to ultrasonography of the abdomen using 3.5 MHZ convex linear and 5.0 MHZ sector transducer on a B-mode real time scanner (Aloka SSD280). Sonographyy for biliary ascariasis was done in various scan planes, including oblique, sub costal, intercostal, transverse, and saggital planes. For intestinal ascariasis the transducer was placed longitudinally and transversally on the anterior abdominal wall, with patient

From the Departments of General Surgery (Mir, Prof. Wani, Shah, Saleem) **and Peadiatric (Rekha) SKIMS, Soura, Srinagar India.**

Received January 1998 Accepted December 1998

Correspondence to : Ishtiyak A. Mir, Department of General Surgery SKIMS, Srinagar.

lying supine. Patients were also scanned in semiupright position. Serial sonographic examinations were done to see for exit of worms from hepatobiliary system, disintegration disappearance of worm masses, and to clinch any complication caused by ascariasis.

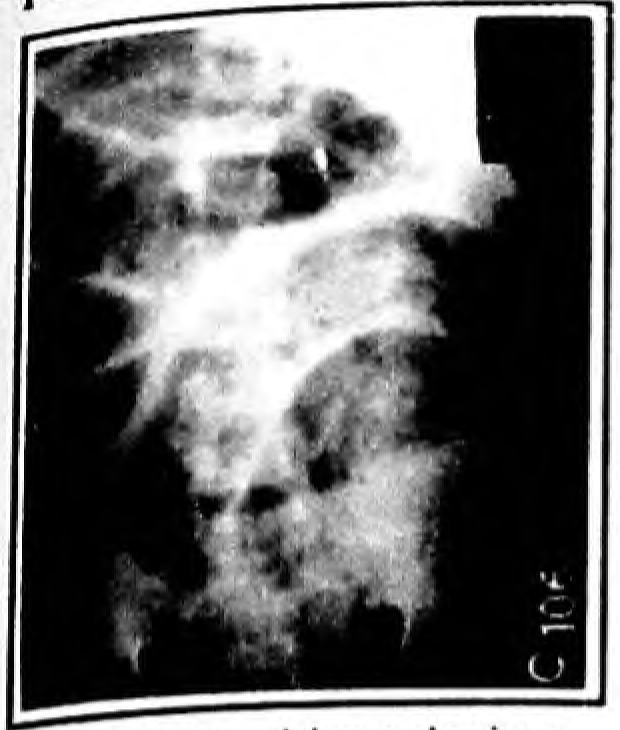


Fig.1: Plain X-ray abdomen showing a segment of the dilated small intesties packed with round worms-Fairly well constrasted against gas in the intestines

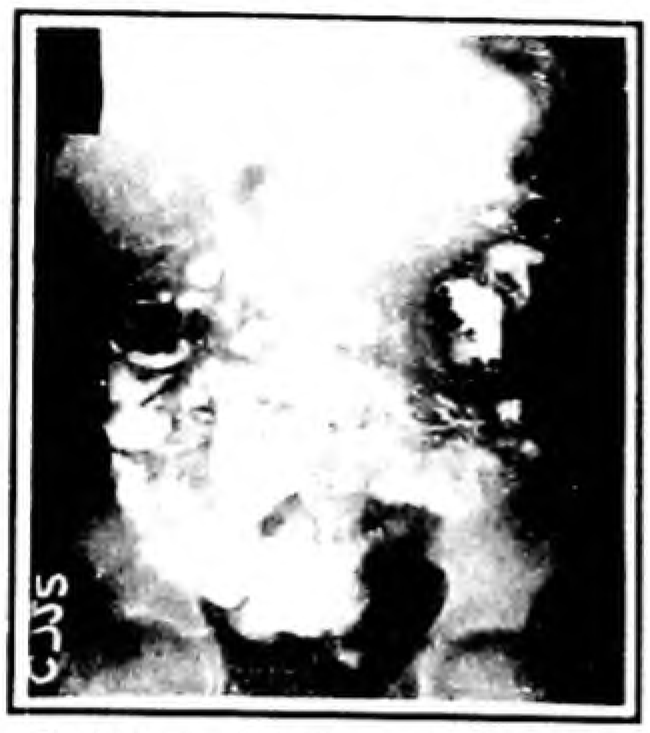


Fig.2: Contrast study examination of the GIT showing cylindrical filling defects resulting in longitudinal translucent area located in the lumen of small intensines

The confirmation that ascariasis is the only cause of ailment was done by taking detailed history. Positive stool sample for ova of ascaris, palpable worm masses which usually disintegrate on conservative treatment, plain radiography of abdomen and contrast study of gut. All the patients managed conservatively passed dozens of worms per rectum. Surgery in 10.00% of the patients revealed features of obstruction secondary to ascariasis.

Results:

In plain radiographs abdomen (table 1) each worm appears as an elongated band of increased density, a few mm in length and of variable curvature. A mass of such worms contrasted against the intestinal gas resembles a group of thick cords. (Fig.1). A distended intestinal loop filled with worms lying side by side gives a whirlpool pattern.

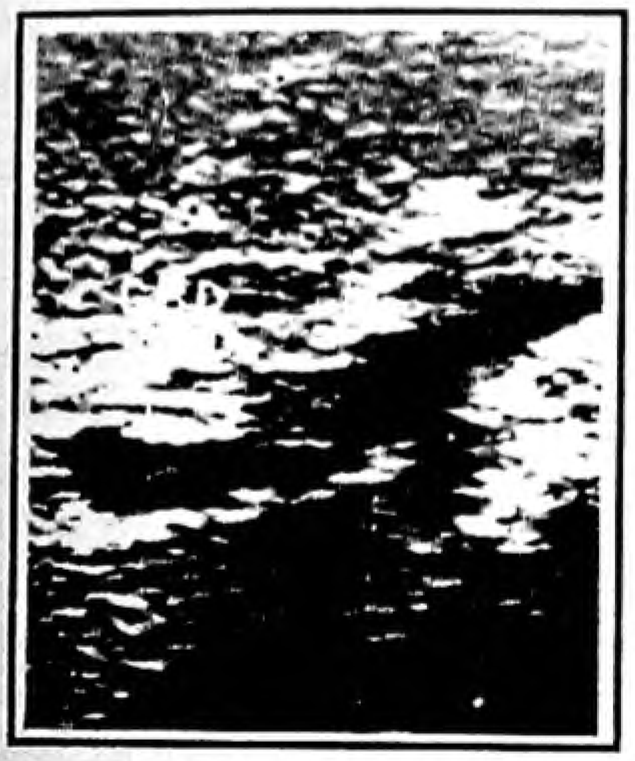


Fig.3 Sonogram revealing a long linear non shadowing ecogenic structure with central anechoic tube representing (Ascaris in CBD) disgestive canal of the worm.

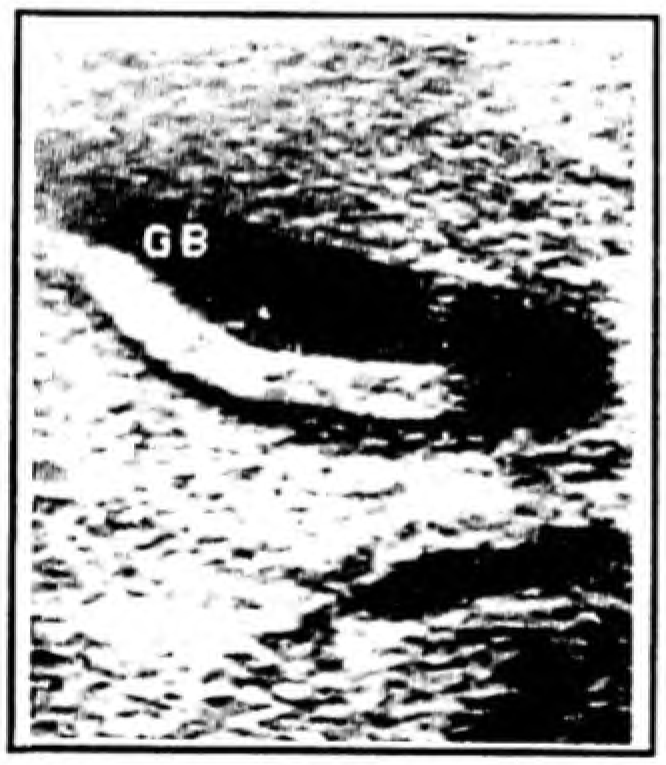


Fig.4 Sonogram revealing tublar echogenic structure with central anechoic tube representing digestive canal of the worm (Ascaris in gall bladder)

Table-I:

Plain radiography finding	Number of patients	Percentage
Bowel distension	92	76.67
Air fluid level	64	53.33
Worm masses	40	33.33
Gasless abdomen	28	23.33
Volvulus	02	01.66
Intussusception	01	00.83.

Note: more than one finding was present in a patient.

Table-2:

Sonographic Finding	Number of pts.	Percentage
Worm masses in gut	28	23.33
Signs of obstruction	16	13.33
Hepatobiliary ascariasis	10	08.34
Free fluid	09	07.50
Freely moving worms	08	06.67
Local collection	01	00.83

Note: more than one finding was present in a patient.

Contrast study showed worm masses in 25 patients (71.42%). Cylindrical filling defects resulting in longitudinal translucent areas located in the lumen of intestines were noted (Fig.2). Ultrasonographic appearance of worms in biliary tract were dilatation of bile duct, presence of long, linear or curved echogenic structures in bile ducts or gall bladder. (Fig.3&4).

Sonographic appearance of worms in intestines were coiled up masses of worms which were hyperechoic and without shadowing in fluid filled segments of the gut. In some patients linear hyperechoic shadows of ascaris in fluid filled coils of gut were noted in cross section.

Disintegration of worm masses and disappearance of worms as seen by serial ultrasound abdominal scans was from 1 to 10 days with a mean duration of 4-6 days. Abdominal sonographic findings are shown in table 2.

Discussion

Delay in diagnosis of surgical ascariasis particularly the complications caused by intestinal ascariasis increases morbidity and mortality. Our findings of plain radiographs closely resemble with Isaac[3] but are at variance with those of Cole[4], Bean[1] and Dasmohapatra et al[5]. Bean[1] had found definite evidence of ascaris in 83.00% of his patients. Waller et al[6] observed gut distension in 64.44% worm masses in 53.55% and air fluid level in 28.8% of their patients closely resembling with present study.

The findings on contrast study in the present series closely resemble with Tracy et al[7], Francke et al[8], Bar Maor[9], but are at variance with those of Lofestrom et al[10], and Dasmohapatra et al[5].

Ultrasonographic diagnosis of biliary ascariasis has been made by Schulman et al[11], Cerri et al[12], Kamath et al[13], Khuroo et al[18] and Hangloo et al[15]. Cerri et al[15] and Khuroo et al[12] emphasised on conducting serial abdominal scans, till the worms disappear from biliary tract. Mean duration of exit of worms in their study was 5 days almost in consistence with present study.

Sonography of intestinal ascariasis has not been reported in literature except one case report by Peck[16]. This is probably because of the fact that worms cannot be detected in gaseous distension of the gut. Sonographic diagnosis of small bowel obstruction by Scheible et al[17] helps in indentifying fluid filled bowel. It is in these fluid filled loops that worms if present can be detected.

All the patients in the present series had features of intestinal obstruction and majority would have been operated, had the sonographic facilities not been available. Though worm masses were detected in only 23.33% and freely moving worms in gut in 7.50% of patients, still only 12 patients were operated. It is believed that mere presence of palpable worm masses, features of intestinal obstruction with out visceral perforation, gangrene volvulus and intussusception, rising pulse rate in absence of any mass and toxaemia out of proportion to the severity of obstruction, does not warrant surgery provided the cause of obstruction is ascaris lumbricoides. It is beyond doubt that in majority of patients the worms distintegrate during conservative treatment and patients get relieved of symptoms. However abdominal scans done at regular intervals when patient is on conservative treatment can pick up some serious surgical complications such as closed loop obstruction where surgery is the only option.

Peck[16] performed ultrasonographic examination of abdomen and within one fluid filled loop four longitudinal lines were seen. In cross section two circles were seen. On these findings Peck suggested diagnosis of ascariasis.

It is hereby concluded that radioimaging helps in subjecting least number of patients to surgery and also the morbidity is decreased in patients undergoing surgery because the surgical intervention is performed in time and in a planned manner.

References:

1. Bean W.J.: Recongimition of ascariasis by routine chest or abdomen roentgnograms. Radiology 1965, Vol. 94; No.2: page 379-384.
2. De Sa A. E: Surgical Ascariasis. Indian Journal of Surgery, 1966, Vol. 28; page 182-190.
3. Isaacs I: Roentgenographic demonstration of intestinal ascariasis in children without using barium. American Journal Roentgenol Radiotherapy and Nuclear Medicine Sep. 1956, Vol.76: No.3: Page 558-561.
4. Cole G.J: Surgical manifestation of ascaris lumbricoides in the intestines. British Journal Surgery, 1965, Vol.52; No.6: page 444-447.
5. Dasmohapatra G.S; Mohanty B: Patnaik G: Clinical appraisal of 200 cases of ascariasis with special reference to surgical complications. Journal Indian Medical Association 1971, Vol.57; No.8: Page 284-287.
6. Waller C.E; Othersen H.B: Ascariasis: Surgical complications in children. The American Journal of Surgery July 1970, Vol.120: 50-54.
7. Tracey M.L; Helden G.O; Bruns H.J: Roentgenographic demonstration of ascaris lumbricoides in the intestinal tract. Gastroenterology, March 1950, Vol.14: No.3: 428-430.
8. Francke W: Roentgenologic findings of small intestines in 100 repatriated prisoners of War. American Journal Roentgenol, Radiotherapy and nuclear Medicine, 1956, Vol 76: No.1: Page 149-152.
9. Bar-Maor J.A; DeCarvalho J.L.A.F.; Chappell J: Gastrograffin treatment of intestinal obstruction due to ascaris lumbricoides. Journal of Pediatric Surgery 1984, Vol.19; No.2: page 174-176.
10. Lofstrom J.E: Koch D.A: The diagnosis of ascaris infestation by serial roentgen examination of the small intestines. American Journal of Roentgenol and Radiotherapy Apr. 1947, Vol.57; No.4: 449-452.
11. Schulman A; Loxton A.J; Heydenrch. J.J: Abdurahman K.E: Sonographic diagnosis of biliary ascariasis. American Journal Radiology, 1982, Vol.139; 485-488.
12. Cerri G.G; Jatobaleite G; Simoes J et al: ultrasonographic evaluation of ascaris in the biliary tract. radiology 1983; Vol. 146; page 753-754.
13. Kamath P.S; Joseph D.C: Chandran R.K; Rao S.R; Prakesh M.L.S.; D'Cruz A.J: Biliary ascariasis: Ultrasonography, endoscopic retrograde cholangio-pancreatography and biliary drainage. Gastroenterology Sep. 1986, Vol. 91; Page 730-732.
14. Khuroo M.S; Zargar S.A: Mahajan R; Bhat R.L; Javid G: Sonographic appearance in biliary ascariasis. Gastroenterology, 1987 Vol.93; Page 267-272.
15. Hangloo V.K: Kaul I: Dev G; Dhar U; Chrungoo R.K; Khan M: Biliary ascariasis. Indian Journal of Gastroenterol 1989, Vol. 8; No.4: Page 265-266.
16. Peck R.J: Ultrasonography of intestinal ascaris. Journal of Clinical Ultrasound. Nov/Dec 1990, Vol.18: page 731-743.
17. Scheible W; Goldberger L.E: Diagnosis of small bowel obstruction: The contribution of diagnostic ultrasound. American Journal of Radiology Oct. 1979, Vol.133; 685-688.

PULMONARY ASPERGILLOMA - SURGICAL MANAGEMENT

A.G.Ahanger, M.Ch.; A.M.Dar, M.Ch.; I.A.Mir, M.S.; N.A. Lone M.D.

Abstract: 31 patients of pulmonary aspergilloma were studied over a period of 8 years. Heamoptysis was the commonest manifestation. Bronchoscopic alveolar lavage and CT scan chest were specific investigations performed. Lobectomy was the commonest surgical procedure undertaken. Wound infection was the commonest post operative complication encountered (14%), suggesting thereby that surgery is the best palliation for management of pulmonary aspergilloma. More than 96% of patients got relieved of symptoms after surgery.

Key words: Aspergilloma, Pulmonary, Heamoptysis

JK-Practitioner 1999; 6(3): 207-210

Introduction:

Fungal infections are at a rise all over the world, inspite of the very broad spectrum antifungal drugs available. This increasing trend is attributed to the abundant use of immunosuppressive and cytotoxic drugs. The most common fungi involving the respiratory tract are: aspergillus, candida and cryptococcus. Different species of aspergillus are residing as nonpathogenic organisms in the normal bronchial tree but can involve the bronchial tree in some preexisting pulmonary lesions.

Pulmonary aspergillosis can be categorised into allergic, invasive or saprophytic infections. The first two are rarely of surgical importance. The third one leads to the formation of pulmonary mycetomas in preexisting lung cysts, cavities or spaces by colonization of the organism. This potentially life threatening fungal ball or aspergilloma is again categorized into a simple and complex-the former being characterized by thin walled cysts lined by endothelium with very little or no surrounding parenchymal lung disease and the latter by thick walled cavities with surrounding parenchymal disease. Tuberculosis is the most common condition associated with aspergilloma but other cavitatory lesions can also be seen associated. these include, sarcoidosis, cavitatory neoplasm, lung abscesses, bronchial cysts, bronchiectasis, cynotic heart disease, pulmonary infarction[1,2].

The commonest manifesting symptom is heamoptysis, the mechanism of its causation is doubtful. One theory attributes bleeding to the mechanical friction of fungal ball with the highly vascular cavity wall. Another school of thought holds that toxins released by the fungus lead to localized hemorrhage. One more theory explains that a heamoptysis secondarily origniates from the inflamed tracheal or bronchial tissue but not from the fungal ball. The other manifestations are; the compression symptoms of a segment, lobe or whole lung by the fungal ball leading to cough, breathlessness, chest discomfort and associated pulmonary infections.

The investigations of aspergilloma have not evolved much as the classical X-ray picture of such lesion has hardly any differential diagnosis although a cavitating neoplasm, infected and debris filled lung cyst can cause some difficulty in the preoperative diagnosis.

Management of such lesions has faced a lot of controversy as still some centers suggest a 'wait and watch' policy for such lesions although a surgical resection of the involved lobe has been advocated by many. Even a very high rate of morbidity and mortality at some centers has not stopped them performing prophylactic resection as advantages of surgery outweigh the complications encountered post operatively. The present study has been conducted with the same benefits in mind and subjecting the patient to surgery.

Material and Methods

During a period of eleven years from June 1985 to August 1996 SK Institute of Medical Sciences, admitted 31 patients of aspergilloma in the department of Thoracic and Cardio-Vascular Surgery. 19 patients were males, 12 were females. Age ranged from 24 years to 68 years with a mean age of 38 years. 29 patients had a history of smoking.

The patients were either reffered from the chest disease hospital, a general hospital or attended the thoracic clinic of our hospital first time. All the patients were symptomatic. The commonest symptoms were productive cough and heamoptysis. Cough was of

From the Department of CVTS SKIMS Soura, Srinagar Kashmir (Ahanger, Dar, Mir) **and Medicine** (Lone)

Received May 1999 **Accepted April 1999**

Correspondence to : Dr. A.G.Ahanger, M.Ch., Asstt. Professor Deptt. of CVTS SKIMS Soura, P.B.No.27 Srinagar-11 Kmr.

chronic nature associated with purulant secretions. It was not responding to antibacterial drugs and cough suppressants. 27% patients had one or more attacks of he amoptysis during the previous years. 22% patients had either completed a nine months course of antitubercular therapy or were still taking the drugs. Six patients had either taken a second course of antitubercular therapy or were receiving it. Three patients were receiving antimitotic drugs for leukemia and sarcoma, two patients had associated bronchogenic carcinoma. Both were squamous cell type. One patient had squamous cell carcinoma left upper lobe, active pulmonary kochs and microbiologically confirmed and radiologically proved aspergilloma.

The patients were labelled to have aspergillus infection by either growing the fungus from bronchoscopically collected specimens or examining the resected lung specimen. Aspergillus Niger was the commonest organism grown. 12 patients were diagnosed before surgery while as rest of the 19 patients showed aspergillus either microbiologically or histopathologically from the resected specimen. twenty percent patients belonged to the category of complex aspergilloma while as 4% patients had simple aspergilloma.

Diagnosis: All the patients were subjected to plain radiography of chest PA and lateral views. It was observed that left upper lobe was involved in most of the patients (56%), followed by left lower. There was evidence of healed tuberculosis in 11 patients with a typical rounded mass in a cavity separated by air. Cavity size ranged from 4-7 cm in longest dimensions. It showed thick walls and surrounding infiltrations[3]. Four patients had calcified spots in the vicinity. Two patients had airfluid levels in the lung fields (Table 1) but one of them bursted into the bronchus as a lung abscess.

Sputum analysis helped to diagnose 12 patients as having aspergillus mycetomas by fungal culture. Sputum was also screened for any bacterial growth and the ones with positive bacterial cultures were treated by specific antibiotics. No sputum sample was positive for malignant cells.

CT scan was performed in nine patients[4,5]. This facility was not available in our hospital before 1990. It showed a clear round mass in a cavity surrounded by air. Although systemic antifungal chemotherapy and local intracavitory instillation of antifungal agents has been tried before but due to poor response, recurrence and increased complications rate[3,6] it was not used in this study. Chronic cough, hemoptysis with indeterminate X-ray shadows on X-ray chest were the indications for surgery.

The surgical treatment given to our patients included lobectomy and pneumonectomy[1]. Dense adhesions was the commonest surgical finding seen in all the patients[1,7]. Left upper lobe was involved in 56% patients followed by left lower lobe (28%) and right upper lobe (16%). The involved area was hard, globular and contained some sand grain like material[4] (Fig.3). In one patient, it was containing foul smelling pus. The same patient had visceral and parietal pleura studed with hard tubercles. He proved to be a case of squamous cell carcinoma associated with aspergilloma and was AFB positive. He was subjected to left pneumonectomy but could not make it postoperatively.

The resected material in all patients was sent for microbiological and histopathological examination. Pleural cavity was as usual drained outside through an intercostal water seal drainage system.

Results:

Twenty one patients had no complications postoperatively. The average hospital stay for these patients was 11.5 days. One of the patients died of obstructive lung disease and CCF 4 years after surgery, rest all are under our follow up. The postoperative complications (Table III) seen in remaining 10 patients were; empyema with bronchopleural fistula in 5, empyema in 3, bleeding in one, wound infection in 5 patients. 3 patients in the same group died[1]. Empyema with bronchopleural fistula was managed by systemic antibiotics and intercostal chest drainage.

Empyema was managed by intercostal drainage, systemic antibiotics to which the organism/s were sensitive and pleural irrigation with povidone iodine. One patient who died on 8th postoperative day after lobectomy was doing well till he studdely drained frank blood in the pleural drain which was put there for drainage of significant serous fluid. He could not be resuscitated even after reexploration. It was seen on re-exploration that a ligature of one of the pulmonary artery branches had given way. The patients with wound infection and stitch abscesses were managed conservatively by wound dressings, except one who demanded secondary suturing of chest wound under general anaesthesia.

All the survivors are under our OPD follow up? One patient had recurrence of hemoptysis. His all the investigations are within normal limits. Four patients needed to be put on antitubercular drugs second time in the immediate postoperative period as evidenced by their microbiological examination of resected specimen.

Thus there were 21 lobectomies, 8 pneumonectomies, and 2 segmentectomies. The resected specimen showed aspergillus in all patients. Three patients had associated squamous cell carcinoma lung, 4 patients grew mycobacteria from the resected specimens. 13 patients were labelled as immunocompromised (2 leukemias, 2 treated squamous cell carcinoma oesophagus, three bronchogenic carcinoma, 6 tuberculosis). Three patients also had bacteremia before operation and sputum culture grew pseudomonas in one, staphylococcus in another and third grew klebsiella. Post-operatively, the pus from empyema or abscesses grew mixed group of oganisms - important ones were streptococci and klebsella.

Table-I: Radiological findings

		R	L	Bilateral
1. Mass lesion	14	5	8	1
2. Typical aspergilloma	11	3	8	0
3. Cavity	3	2	1	0
4. Empyema	1	1	0	0
5. Diffuse infiltrates	5	0	0	1
6. Bronchiectasis	7	4	3	2

Table-II: Indications/Surgery

		%
1. Heamoptysis	13	41.93
2. Chronic cough	8	25.80
3. Indeterminate mass	6	19.35
4. Empyema with conolidation of lung	1	3.22
5. Collapse of lung	3	9.66

Table-III: Complications encountered

	%
1. Wound infection	5
2. Boronchopleural fistula with empyema	5
3. Isolated empyema	3
4. Bleeding	1
5. Bacteremia	3
6. Death	3

Note: More than one complications occured in one patient. Total number of patients with post. operative complications were 10.

Discussion:

Although the infection with aspergillus is uncommon and even if it occurs it has low pathogenicity but in cases of reduced immunity by any reasons, the organism becomes highly pathogenic[2] and invades any organ[2].

Involvement of the lungs has seen in most of the instances. Lungs get involved either by the formation of dormant localized fungal ball -a mycetoma or there occurs invasive pulmonary aspergillosis[1,8].

A third variety of this infection can present as bronchial aspergillosis which is a non invasive fungal infection characterized by cough, fever, wheezing and eosinophillia[1,7].

In the present series the patients who had already completed their course of antitubercular therapy or were taking it, patients of different malignancies like leukemias[1], bronchogenic carcinomas, oesophageal carcinoma and also some diabetics who presented with different chest symptoms and signs were evaluated[6]. Hemoptysis was the commonest symptom of these patient (41.95%). In some of the patients it had recurred after the full course of antitubercular therapy while in others, it had not stopped even after the chemotherapy. 18 patients had massive and significant hemoptysis (>500ml/24 hours) several times within a period of 2-3 months. They responded to conservative medical management.

Chronic cough was another major complaint of most of our patients[6] (25.72%). It was dry in 8.25% and productive in 17.5% of patients. The secretions were mucopurulant, purulant or hemmorhagic[9]. Very few (9.27%) had fever, weight loss or anorexia[4]. One patient presented with hemothorax, purulant cough and hemoptysis. Another patient had left empyema thoracis with an aspergilloma of left mid zone[1]. A third patient presented with bronchiectasis and a mass shadow left apical zone, he was a kyphoscolotic.

The age of the patients was always more than 24 years[4]. The oldest patient seen was a 68 years old female.

Diagnosis was made by plain radiography of the chest, analysis of bronchoscopically collected aspirate[1], CT scan of the chest and of course in all cases confirmed by peroperative observations and histopathological examination of the specimen, although AK Trull et al[1] reported that culturing aspergillus from the different body specimens is very difficult before death.

X-ray of the chest revealed an indefinite mass lesion in 96.4% of patients[3], cavitatory lesions in 9.86% of patients. Pleural collection (empyema) was seen in one patient (3.21%). There were diffuse pulmonary infiltrates in 28.67% of patients and 9.63% had associated bronchiectasis. The side of involvement was more often left than the right side. The site of involvement was left upper zone in most of patients (56%). As most of the patients had post-tubercular aspergilloma, the radiological findings were the sequalre of tuberculosis like bronchiectasis and cavitatory lesions.

As mentioned by Richard et al[2] 1983[4], a CT scan chest is a superior radiological investigation than routine radiography or standard tomography in chest lesions. We have also been helped by the same tool but in a very few patients where it was available especially in doubtful cases of indeterminate mass lesions gives a typical picture of a rounded ball in a cavity surrounded by air. It should be investigation of choice after x-ray chest.

Bronchoalveolar lavage collected endoscopically was positive for aspergillus in only 12 patients, may be the cavity was not communicating with the bronchus. 3 patients were diagnosed as having bronchial malignancy from the resected specimen. Richard C. Daly et al[9] have also noticed a 4% association of bronchogenic carcinoma with aspergilloma. One patient had treated squamous cell carcinoma of oesophagus. Two patients had associated leukemia of CL type. Indication of operation was recurrent hemoptysis and/or doubtful shadow on x-ray. James et al[7] have operated the patients of recurrent hemoptysis, life threatening hemoptysis, chronic cough and progressive infiltrates around a cavity in cases of aspergilloma. Richard et al[4] recommended empyema, bronchoplural fistula, pulmonary abscess, indeterminate mass as an indication of operation[1] for aspergilloma besides hemoptysis and cough.

As reported by Lin, thoracotomy was difficult because of pleural space obliteration. He also mentioned that lung resection was the commonest operation performed. In the present study similarly lot of adhesions were observed to reach the hilum or the aspergilloma, so we only performed resection of lung tissue along with aspergilloma and in some cases drainage of empyema with decortication. No wedge resection, cavernostomy or thoracoplasty was performed, no bony encroachment or mediastinal involvement was seen on thoracotomy as reported by David K. Wagner et al[3]. In two patients, the superior wall of the cavity could not be mobilized hence was diathermized and left behind. 200 ml of 5% betadine solution was left in such pleural cavities for 4 hours postoperatively in both these patients are doing well postoperatively. None of the patients was put on any antifungal treatment. Pleural cavity was always washed with 10% betadine if there was any dissemination with the sand grains of fungus ball.

Post operatively, four patients needed ventilatory support. All these patients had undergone pneumonectomy and had poor lung functions (VC<2 liters). One of these scummbed to death due to septiceamia and multiorgan failure. One patient demanded emergency pneumonectomy due to massive heamoptysis and drainage of non resolving lung abscess. He also had associated squamous cell carcinoma.

The complications encountered were more with complex aspergillomas. Three deaths, besides septicemia in two patients, bronchopleural fistual in three, empyema in one, wound infection in 5, dehiscence in one. Simple aspergilloma did not show much complications. No patient died in this group. The major complications encountered were empyema in one and wound dehiscence in one.

Resected specimens were positive for aspergillus in all, positive for AFB in 4, for malignant cells in one and the bacteria in 13. We thus conclude:

1. The indeterminate mass lesion should always be evaluated/explored to rule out aspergilloma/ malignancy.
2. CT chest should be included in the battery of investigations for evaluating aspergilloma on priority.
3. Systemic chemotherapy is not needed after resection of aspergilloma.
4. Surgical resection should outweigh the local or systemic antifungal therapy for aspergilloma treatment.

References:

1. A.K. Trull, J. Parker, R.E. Warren. IgG enzyme linkied immunosorbent assay for diagnosis of invasive aspergillosis: retrospective study over 15 years of transplant recipients. J. Clin. patho. 1985;38:1045-1051.
2. A.P.Boon, D.O'Brien, D.H. Adams. 10 years review of invasive aspergillosis detected at necropsy. J. Clin. Pathology 1991; 44: 452-454.
3. David K. Wanger, Basil Varkey, Neela K.Sheth, Gary J. Damort. Epidural abscess, vertebral distruction, and paraplegia could be extended infection from an aspergilloma. The American Journal of Medicine, March 1985;78:518-522.
4. Richard A. Glimp, Arnold S. Bayer. Pulmonary aspergilloma: Diagnostic and therapeutic considerations. Arch Int. Med. 143, Feb.1983: 303-308.
5. Winfield J. Wells, Arther H. Fox, Pierre R. Thiodore-Aspergillosis of posterior mediastnum. Ann Thorac Surg 1994;57:1240-1243.
6. Ralpha O. Butz, James R. Aventina and Bernard J. Leiniger. Ten years experience with mycetomas in patients with pulmonary tuberculosis. Chest 87/3/March,1985;465-358.
7. James W. Battagilini, G.F. Murray, B.A.Keagy et al. Surgical management of pulmonary aspergilloma. The Annals of Thoracic Surgery 1985;39,6:512-516.
8. G.R.Park, D.Lamp. J.R. Milne et al. Disseminated aspergilloosis occuring in patients with respiratory, renal and hepatic failure. The Lancet July 24, 1982;179-183.
9. Richard C. Baby, Reter C. Pairolero, Jeffrey M. Rishler et al. Pulmonary aspergilloma: Results of surgidal treatment.J. Thoracic Cardiovasc Surg.95:981-988, 1986.

ELECTROENCEPHLOGRAPHIC CHANGES IN MIGRAINE - A STUDY OF 200 CASES

S.K. Gupta M.D.; Ashok Parihar M.D.; Hardev Gupta M.D.

Abstract: In the present study Electroencephalographic change (EEG) were recorded in 200 patients of migraine and in 50 healthy individuals which served as controls. 35% of EEG records were abnormal in migraine where as 8% were abnormal in controls. In migraine group out of 35% abnormal records, 51% have slow wave abnormality either unilaterally or bilaterally and remaining 49% revealed sharp waves and spikes. Amongst the control group 4% had slow waves and equal number had sharp waves. In the migraine group 12% of the records also revealed fast beta rthythm in the frontal regions which is associated with stress of patients keeping tense during the recording.

The epilepsy has a definite relation to migraine as revealed by sharp waves and spikes in patients of migraine. The sharp waves have been recorded diffusely and bilaterally presenting as dysarrhythmia. Activating procedures like hyper-ventilation and photic stimulation did not reveal any exaggeration of EEG changes in migraine or control groups. The patients with EEG abnormalities responded well to anticonvulsants like phenobarbitone.

Key words: Migraine, epilepsy, E.E.G. Changes.

JK-Practioner 1999; 6(3): 211-214

Introduction:

Headache is the most common complaint in OPD patients and approximately 12% of patients suffer from vascular headache as reported by Salby and Lance 1960[1]. There are many different kinds of headache. Adhoc committee of U.S. National Institute of Neurological and Communication Disorders and Stroke classified headache disorder and provided short description of various syndromes in 1962[2]. Later on in 1988 International Headache Society has published an extensive document which has now formed the basis of classification of headache[3].

The exact definition of migraine syndrome is debatable and difficult and all patients will not fall within the narrow concept of paroxysmal disturbances of cerebral function associated with headache and vomiting. The migraine is a vascular disorder consisting of two separate phases. In phase I, there is intracranial vasoconstriction followed by extracranial vasodilatation in phase II. The attack of migraine may be produced by phase II or a combination of both. The term migraine is derived from hemicrania means the patient usually feels unilateral headache, but is not unusual to have pain over the entire head with or without accompanying symptoms. The essential character of these vascular headaches is their paroxysmal nature.

The EEG abnormalities in patients of headache in general varies from 15-20% in various studies which almost equal in number to EEG recordings in normal population without headache. EEG in migraine shows alpha rhythm abnormalities, slow waves and sharp waves or spikes which range between 30-40% of the migraine cases[4]. Though specific EEG changes in migraine are lacking.

Classification of Headache:

The headache was classified by adhoc committee on Classification of Headache 1962[2]. The criteria for classification of headache has served as a framework for diagnosis for major clinical types of headaches and offered a logical approach to the planning of therapeutic trials and served as a basis for research in headache.

1. **Vascular Headaches of migraine type:**
    a. Classical migraine.
    b. Common migraine
    c. Cluster headache.
    d. Hemiplegic & ophthalmoplegic mirgraine.
    e. Lower half headache.
2. Muscle contraction headache.
3. Combined headache (Vascular and muscle contraction).
4. Headache of delusional, conversion of hypochondrical states.
5. Headache of nasal vasomotor reaction.
6. Non migrainous vascular headache.
7. Traction headache.
8. Headache due to overt cranial inflammation.

From the Department of Neurology (Gupta, Hardev) **and Medicine** (Prof. Parihar)**Govt. Medical College Jammu.**

Received August 1998 Accepted January 1999

Correspondence to : Dr. S.K. Gupta (Neurologist) 718-A, Gandhinagar Jammu-Tawi-180004 J&K.

9. Headache due to diseases of ocular aural, nasal, dental or other cranial or neck structures.
10. Cranial neuritides.
11. Cranial neuralgias.

Jes Olsen in 1990[3] published an extensive document which formed the basis of classification of headache in the New International Classification of disease by W.H.O. which was supported by World Federation of Neurology Research group on migraine and headache and American Association for Study of Headache. According to this classification, the following types of headaches have been described.

1. **Migraine:-**
   - a. Migrane without aura.
   - b. Migraine with aura.
     - i) Migraine with typical aura
     - ii) Migraine with prolonged aura
     - iii) Familial hemiplegic migraine
     - iv) Basilar migraine
     - v) Migaine aura without headache
     - vi) Migraine with acute onset aura.
   - c. Ophthalmoplegic migraine.
   - d. Retinal Migraine
   - e. Childhood periodic syndromes that may be precursors to or associated with migraine.
     - i) Benign paroxysmal vertigo of childhood.
     - ii) Alternating hemiplegia of childhood.
   - f. Complications of migraine.
     - i) Status of migrainous
     - ii) Migrainous infarction
   - g. Migrainous disorders with fulfilling above criteria.
2. **Tension Type headaches:-**
   - a. Episodic tension type headache.
     - i) Episodic tension type headache associated with disorders of pericranial muscles.
     - ii) Chronic tension type headache unassociated with disorders of pericranial muscles.
   - c) Headache of tension type and not fulfilling above criteria.
3. **Cluster headache and chronic paroxysmal hemicrania.**
4. **Miscellaneous headaches unassociated with structural lesions.**
   - i) Idiopathic throbbing headache.
   - ii) External compression headache.
   - iii) Cold stimulus headache.
   - iv) Benign cough headache.
   - v) Benign exertional headache
   - vi) Headache associated with sexual activity.

Diagnostic criteria for migrainous type of headache by International Headache Society.

1. **Migraine without aura.**
   - a. At least 5 attacks fulling B-D.
   - b. Headache attack lasting 4-72 hours (untreated) or unsuccessfully treated.
   - c. Headache has any two of the characteristics.
     - i) Unilateral location.
     - ii) Pulsating quality.
     - iii) Moderate or severe intensity.
     - iv) Aggravation by walking stairs or simple routine physical activity.
   - d. During headache at least one of the following:
     - i) Nausea and or vomiting.
     - ii) Photophobia and phonophobia.
2. **Migraine with aura.**
   - a. At least 2 attacks fulfilling B.
   - b. At least 3 of the following four characteristics:-
     - i) One or more fully reversible aura symptoms indicating focal cerebral, cortical and or brain stem dysfunction.
     - ii) At least one more symptom develops gradually over 4 minutes or 2 or more symptoms occur in succession.
     - iii) No aura and symptoms last more than 60 minutes if more than one aura, symptom is presented, accepted duration is proportionally increased.
     - iv) Headache follows aura with free interval or less than 60 minutes (it may also begin before or simultaneously with aura).

Material and Methods:

The material for the present study was taken from Neurology Section of Governement Medical College Jammu. The diagnosis of migraine was made on the criteria laid down by the International Headache Society (1990)[3]. A total of 200 cases of migraine were studied for EEG changes.

All patients underwent a detailed history and clinical examination. Patients with history of head trauma, seizure disorder, hypertension, sinusitis or focal neurological deficit were not included in the study. Each patient underwent routine investigation including haemogram, X-ray skull, X-ray PNS, fundus examination and C.T. Scan of head in those cases where a clinical suspicion of organic brain lesion was high, to exclude it from the study.

EEG was done in all the cases and recording was made on 16 channel EEG machine with following specification.

Sensitivity - 7.5 mm = 50 uv
Paper speed - 30 mm/sec.

Electrodes - surface.

Both unipolar and bipolar recordings were done and follwing activation procedures were used:-

- Photic stimulation
- hyperventilation

Care was taken to remove artifacts by using appropriate filter. A group of 50 healthy indifviduals were also studied which served as controls.

Observations:-

The present study consists of two hundred cases of migraine who were subjected to EEG recordings and 50 healthy individuals were also studied who served as controls. The following observations were made:-

There were 76 males and 124 females and age group ranged between 10 to 50 years. The majority of patients were in the age group of 15 to 40 years. The youngest case was 10 years and oldest 60 years of age. The frequency of attacks in these patients is shown in the following table-I.

Table-I:

Frequency of attacks in months.	No. of cases	Percentage
< 1	10	4
1-3	114	57
4-6	68	34
>6	10	5

The duration of headache persisting during the attack was less than 6 hours in 30% of cases, 6-24 hours in 35% of cases. 24-48 hours in 27% and only in 8% of the patients the duration of headache was more than 48 hours. In 67% of patients, the headache was hemicranial and in 33% it was holocranial. The aura preceding headache was present in 15% of the cases in the form of visual disturbances. Nausea was present in 76% and vomiting in 35% of cases. Photophobia or phonophobia was seen in about 8% of the cases. Family history of headache was present in 34% and emotional stress in 23% of the patients.

EEG changes in migraine:

The EEGs recorded in 200 patients of migraine were normal in 65% of the patients and abnormal in35% only. Various abnormalities reported were slow waves in 51% and sharp waves in 49%. These abnormalities were seen either unilaterally or bilaterally, focal or diffuse in the parieto-occipital region or occipital regions.

Discussion:-

In the present study two hundred cases of migraine and 50 healthy individuals were studied for various EEG abnormalities. The healthy individuals served as controls.

As many as 92% of the EEG records in healthy individuals were normal and only 8% of the records were abnormal. There is a general consensus that electroencephalographic abnormalities do persist in 15-20% of the normal population. In the present study percentage of abnormal records in healthy group had been quite low i.e. 8% as compared to 15-20% as described by various workers[5,6,7]. In the control group abnormality was of slow and sharp waves.

EEG changes in Migraine group:-

In migraine group 35% of patients had abnormal EEG records as compared to normal controls. This proves that patients with migraine have higher prevalence of EEG abnormality compared with general population and this difference is quite significant statistically.

Amongst 200 cases of migraine 35% of patients had abnormal records, out of which 51% had slow waves and 49% had sharp waves, and spikes. The table II shows the percentage of abnormal EEG records in migraine amongst various series:-

Table-II

Name of Author	Year	Percentag of abnormal records
Dow and Whitty[6]	1947	50
Chon[7]	1948	41
Strauss and Selinzki[8]	1949	43
Weil[9]	1952	26
Heyek[10]	1956	29
Panzani[11]	1959	60
Salby and Lance[1]	1960	30
Carter and Leary[12]	1960	33
Smith & Winter[13]	1964	31
Gill et al[14]	1966	22
Hockday and Whitty[15]	1969	60
Loger and Fazekas[16]	1986	60
Present study	1997	35

The abnormal EEG records demonstrated by various authors have been in the range of 22-60%. Weil in 1952[9] described spike and sharp wave abnormalities in patients of migraine. Engel et al[17] demonstrated slow waves during an attack of scotoma i.e. classical migraine. They also demonstrated disappearance of these changes with disappearance of the scotoma. Cohn[7] also demonstrated similar changes in patients with scotoma but all these EEGs were recorded during headache free period. So in Chon's study EEG changes persisted even after disappearance of the scotoma. In the present study aura was seen in 30 cases and EEGs were recorded during headache free period. All these cases revealed slow waves. Our findings do coinside with well and Cohn but EEG changes has not disappeared after disappearance of aura as reported by the Engel et al[17].

Various authors have described slow waves in simple migraine or migraine without aura. Dow and Whitty[6] and Weil[9] reported slow wave in 50% and also theta rhythm abnormality in 50% of cases. Slow wave activity was also reported by Heyek[10], Salby and Lance[1], who also reported positive spikes. Rausenbaum and Merrit[18], Slaghter[19], Hockday and Whitty[15], Wasley and Goldenberg[20] have reported slow waves in more than 50% of their abnormal records. In the present study also slow waves were seen in 515 of the abnormal cases and most of these had been in the focal distribution.

In the present study 49% of the abnormal records revealed sharp waves and spikes either unilaterally or bilaterally. The similar changes are being reported by others like - Weil[9], Krapp and Friedman[21], Salby and Lance[1], Carter and Leary[12]. They have reported sharp wave and spikes and called it as pathological dysarrythmia. Smith and Winter[13] reported spikes in nonepileptics and epileptics with headache. Salghter[19] and Hockday and Whitty[15] reported cerebral dysarrythmia with positive spikes in patients with migraine. Bilateral dysarrythmia was also reported by Wasley and Goldenberg[20]. The patients of migraine who showed these spikes and sharp wave changes, were labelled as dysarrythmic migraine which has been originally described by Weil[22-23]. Such dysarrythmia is also present in patients with epilepsy. Simith and Winter[13] has studied EEG changes in both epileptics and nonepileptics with headache and found sharp waves and spikes in both the groups and treated the non epileptics with headache with anti-convulsants. Response to anti-convulants made them to believe that in some of the patients of epilepsy headache may be the only manifestation responding to anticonvulsants. Other authors also treated such patients of migraine with sharp waves and spikes with anticonvulsants thinking that the dysarrythmic migraine may be a type of epilepsy. In the present study these patients of migraine who had spike and sharp wave discharges were not responding to convenional treatment and their frequency of attacks was much more as compared to other patients once they were started with 60 mgms/day dose of phenobarbitone which was continued for a year and out of 34 patients who had sharp waves and spikes in the present study, 30 became symptom free which was quite significant.

The authors suggest that those patients of migraine who has frequent attacks and severity of attacks increases despite usual medication one should go for EEG and if there is any dysarrythmia these patients should be given anticonvulsants thinking them as a dysarrythmic migraine.

References:

1. Salby, G and Lance, J.W. EEG changes in Migraine J. Neurol Neurosurgery, Psy. 1960, 23: 23-32.
2. Adhoc Committee on Classification of Headache. Classification of Headache. JAMA, March 1962 p.717-718.
3. Jes Olesen M.D. Classification and diagnosis of headache disorders. Neurology Clinics 1990; 8(4): 793-798.
4. Akimoto H. EEG Studies in Migraine. In J. Neurol 1962, 3: 379-387.
5. Camp W.A. and Wolff H.G. Studies on headache Arch Neurology Chicago, 1961, 4:475-478.
6. Dow, D.J. and Whitty C. W.H. EEG and migraine. Lencet, 1947,2:52-57.
7. Cohn, R. Clinical Electroencephalography New York McGraw Books Company Ire. 1949:p.493-497.
8. Strauss, H. and Selinzki H. EEG findings in patients with migrainous syndrome. Traus Amer neurol. Ass. 1949;67:205-209.
9. Weil A.A. EEG findings in Psychosomatic headache and dysarrythmic migraine./Electroencephalo-clin Neurophysiol. 1952; 4:181-186.
10. Heyek H Neue Beitrage Viv Klinik and Pathogens de rmigraine. Stutgart George Thieme Verlag 1956 p. 171-174.
11. Panzani, R. EEG changes in migraine and bronchial asthma. Int. Arch. Allergy 1959;15:141-147.
12. Carter, F.W.A. and Leary O.C.C. Headache in childhood. EEG evaluation of 500 cases. Neurology, 1960;10:839-42.
13. Smith, V.O.G. and Winter, A.L. EEG in Migraine . Electro encephalography and clinical Neurophysiol. 1964; 16: 194-202.
14. Gill, R.D., Valieger, M. and Van-Valiet, A.G.M. Headache and EEG. Electroencephalo clinic Neurophysiol 1966;21:492-95.
15. Hockday and Whitty C.W.M. A Study of 100 patients of migraine. Br. Med. Journal 1968;1:735-36.
16. Logar, C. and Fazekas, F. EEG-EMG electro encephalography Verwandt. Geb. Sept 1986;17(3):153-56.
17. Engel, G.L., Ferris, E.B. and Romano Focal EEG changes during scotoma of migraine. American J. Med. Sciences 1945;249: 750-57.
18. Rausenbaum, A.P. and Merrit H.H. Familial Hemiplegic migraine. Neurology, 1960;10:164-169.
19. Slaghter, K.H. Some clinical and EEG findings in migraine. Brain, 1968, 91:p.85-98.
20. Wasley, P.M.N. an goldenberg G. EEG, EMG Electroencephalograph Vorwandta Geb. 1985(Dec.); 16(4):221-26.
21. Krupp, G.R. and Friedman A.P. Recurent headache in children - a study of 1000 cases. New York J. Med. 1953;53:43-46.
22. Weil A.A. Dysarrythmic migraine. Olio St. Medical Journal 1954;50: 668-671.
23. Weil, A.A. Observation on Dysarrythmic migraine. J. Nervement Disease 1962, 134: 227-28.

HEMODYNAMIC AND VENTILATORY CHANGES DURING LAPAROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA

Akhtar Naqib MD; Saleema Mir MD; Syeed Qazi MD.

Abstract: *The haemodynamic and ventilatory changes during balanced anaesthesia were studied in 25 patients after peritoneal insufflation of carbon dioxide. Intra-operative monitoring included heart rate blood pressure, central venous pressure, airway pressure endtidal carbon dioxide (Et Co_2), oxygen saturation (SPo_2) and arterial blood gases. The study showed that there was statistically significant rise in heart rate after 10 minutes. 10, 20, 30 and 40 minutes after insufflation, there was also increase in systolic blood pressure. We also observed a significant rise in $PaCo_2$ with Co_2 insufflation. Oxygen saturation remained always more than 95% in all patients. All parameters returned to pre-insufflation values following decompression of abdomen.*

Key words: *Monitoring $EtCo_2$ $PaCo_2$, Pulse Oximeter, Laproscopy, Cholecystectomy.*

JK-Practitioner 1999; 6(3): 215-217

Upper abdominal surgery is associated with postoperative pulmonary dysfunction in upto 48% of patients[1] Impaired diagraphmatic function, type of skin incision, postoperative pain, muscle paralysis and decreased functional residual capacity have all been found to contribute to postoperative pulmonary dysfunction.[2,4] Laparocospic cholecystectomy has become the treatment of choice for many patients with symptomatic cholelithiasis. The advantages of laparoscopic cholecystectomy over traditional open cholecystectomy include limited postoperative pain, shorter hospitalization, earlier resumption of activity and the proved consmesis.[5-7] The creation of pneumoperitoneum which is an essential pre requisite for any laparoscopic procedure can cause serious physiological disturbances. Today carbon dioxide (Co_2), the gas of choice for producing pneumoperitoneum with associated postural changes needed for the procedure, can cause severe potentially harmful haemodynamic and respiratory consequences. Since laparoscopic cholecystectomy recently has become a widely used surgical technique, it has been reported that an insufflation of Co_2 into the abdominal cavity has changes on haemodynamic, ventilatory and acid base status of these patients. It is mandatory to have data on these changes during general anaesthesia.

Material and Methods

Thirty five patients undergoing laparascopic cholecystectomy were included in the study after being approved by the institutional ethics committee and informed consent was obtained from each patient. The patients were between 25 and 65 years, of age and were ASA status I. No. patient had cardiovascular, respiratory or cerebrovascular disease. In addition none had received any medication. No premedication was given to any patient. In the operation theatre peripheral intravenous access was established and 300 ugm of Buprenorphine was given to all the patients I.V. before induction. Anaesthesia was induced with thiopentone 4-5 mg/Kg I.V. and endotracheal intubation was facilitated with suxamethonium 1-2 mg/Kg I.V. Anaesthesia was maintained with oxygen (33%), Nitrous Oxide (66%) and pancuronium and patients were mechanically ventilated on the controlled mode at a constant tidal volume and frequency throughout the study. The left radial artery was cannulated for direct monitoring of arterial blood pressure and arterial blood gas analysis. Right internal jugular vein was cannulated to measure central venous pressure. In addition continuous ECG, heart rate, SPo_2 and $EtCo_2$ was monitored in all the patients.

All the patients were operated in supine position and abdomen of each patient was insufflated with 100% carbon dioxide until the intra abdominal pressure reached 14 mm Hg. The intra abdominal pressure was maintained at 14 mm Hg with a flow rate of 1-2 litres per minute. All the parameters were measured before insufflation and till 40, 50, 60 minutes after insufflation with head up tilt and finally 10 minutes after ex-sufflation. After the end of surgery the neuromuscular block was reversed with neostigmine 0.08 mg/Kg and atropine 0.02 mg/Kg.

From the Department of Anaesthesiology, SKIMS, Soura Srinagar, India (Naqib, Mir, Qazi)

Received February 1998 Accepted December 1998

Correspondence to : Dr. Akhtar Naqib, Deptt. of Anaesthesia, SKIMS, Srinagar, Kashmir

(Table-I) Ventilatory And Blood Gas Changes

	Before Insufflation	After 10 min.	After 20 min.	After 30 min.	After 40 min.	After 50 min.	After 60 min.	End of Co_2 Insufflation
PH	7.44±0.02	7.40±0.04	7.37±04	7.35±0.04	7.28±0.04	7.35±0.02	7.25±0.04	7.36±0.05
$PaCo_2$	36.4±2.6	38.5±3.5	40.9±5.6	42.8±5.6	43.6±4.6	44.2±4.6	44.8±5.4	37.20±5.7
HCo_3 (meq/L)	24.3±1.8	24.6±1.4	24.4±1.8	24.2±1.6	24.4±1.2	23.8±2.2	24.6±1.6	24.2±1.8
BE (meq/L)	1.4±1.6	0.5±1.6	-0.4±1.5	-0.9±1.4	-1.2±1.5	-1.6±1.4	-1.7±1.5	-1.2±1.6
AWP	18.80±1.46	20.20±1.42	24-04±1.62	26.05±1.64	26.08±1.72	26-16±1.74	26-20±1.76	18-20±1.42
$ETCo_2$ mmHG	34.46±2.42	34.82±2.48	36.10±2.64	38.64±2.86	38-76±3.44	38.68±4.24	38.40±4.44	34.60±2.72

Meanm±SD $P<0.05$ $P<0.001$

When spontaneous breathing resumed patients were extubated and transferred to the recovery room.

Statistical difference was determined by two-way analysis of variance to compare pre-insufflation changes with post-insufflation values and a probability of 'P' value of less than 0.05 was regarded as statistically significant.

Results

All the patients were similar with respect to ASA classification, age, weight and duration of the operation. Heart rate, systolic and diastolic pressure increased significantly ($P<0.5$) 30 min. after Co_2 insufflation into the abdominal cavity compared to pre-insufflation value.

CVP also increased significantly ($P<0.001$) following the pnemoperitoneum and with head up position and this value remained high through out the insufflation period. Table-I. End-tidal Co_2 during insufflation increased significantly and continued to increase slowly throughout the procedure. No significant change was observed in $PaCo_2$ and SPO_2 in any patient. pH decreased significantly during Co_2 insufflation ($P<0.01$) and $PaCo_2$ increased significantly ($P<0.01$). Airway pressure increased significantly after insufflation and remained high during the remainder of the insufflation period. All the parameters returned to normal soon after the deflation of the peritonial cavity. Table-II.

Discussion:

Laparascopic cholecystectomy has replaced the operatove procedure as the gold standard[11-12]. Laparascopic cholecystectomy was introduced by Dubios et al[13] in France in 1987. After initial skepticis in this procedure has gained widespread popularity and is now described as the procedure of choice for symptomatic Cholelithiasis. In the current surgical dictum, the term laparoscopy implies the use of carbon dioxide pneumoperitonium to provide exposure for adequate visualisation of the viscera. While pneumoperitoneum is effective in providing exposure, significant ventilatory hemodynamic and metabolic alterations are associated with the intraperitonial insufflation of carbon dioxide. Arterial partial pressure of carbon dioxide and End-tidal Co_2 levels increase in a consistent manner[14]. This phenomenon does not present significant difficulties in the majority of healthy patients but may seriously complicate the perioperative course of patients with obstructive pulmonary disease. Walfe et al[15] and Wittgen

(Table-II) Haemodynamic Changes (Mean±SD)

	Before Insufflation	After 10 min.	After 20 min.	After 30 min.	After 40 min.	After 50 min.	After 60 min.	End of Co_2 Insufflation
Heart rate (Beats/min)	74±4	78±64	80±4	82±2	82±6	80±6	78±2	76±2
Sytolic BP mmHG	120±4	125±2	130±2	135±4	135±6	130±8	130±2	125±4
Diaslotic BP mmHG	70±8	75±6	80±4	80±4	84±4	80±6	75±4	70±2
CVP	2.5±4	5.6±4	6.0±2	6.4±4	6.6±2	6.4±1	5.5±2	3.2±2

$P<0.05$ $P<0.001$

et al[16] described patients with severe Co_2 retention who needed prolonged mechanical ventilation after surgery.

The results of this study indicate that Co_2 insufflation upto 15 mm Hg induces significant haemodynamic and ventilatory changes in ASA I patients. In all patients we observed a significant increase in heart rate and blood pressure within ten minutes following Co_2 insufflation, similar changes have been reported earlier also[17]. These changes have been thought to be caused by the increased sympathetic activity because the return to normal heart rate does not immediately follow the evacuation of the pneumoperitoneum but reflects the time needed to wash the catecholamines out of the circulation[18]. Other factors which are responsible for hemodynamic changes are increase in systemic vascular resistance, predominant increase in systemic nerve activity as a result of afferent stimulation from Splanchic region due to Abdominal distension, increased venous return and consequent increase in cardiac output, hypercarbia and activation of renin angiotensin mechanism[19].

Pneumoperitoneum significantly increases CVP and airway pressure. Previous studies have shown a signifcant rise in CVP because of increase in ventricular filling pressure during pneumoperitoneum by auto-transfusion of pooled venous blood from splanchnic region[10-20]. The increase in AWP is attributed to increase in intrathoracic pressure[14,15]. The data of our study confirms this.

References:

1. Craig B.O. Post operative pulmonary function Anesth Anagl 1981; 160: 46-52.
2. Wahba RUM. Peri operative functional residual capacity Can. J. Anasth 1991; 38: 384-400.
3. Ali J. Weisel RD. layug AB, Kripke by Hechth on HB. consequences of post operative alteration in respiratory mechanics.
4. Ali J. Khan TA, The Comparative effects of muscle transection and median upeer abd. incision on post operative pulmonary function. Sug. Liyheal obst 1979; 148: 1863-6.
5. Graves HA, Ballinger JF, Anderson WJ. Appraisal of Laparoscopic Cholecystectomy. Ann. Surg 1995; 213: 655-64.
6. Schirmen BD, Edge SH, Dix Y, Hyser MJ, Hanks JB, Jones Rs. Laparoscopic Cholecystectomy treatment of choice for symptomatic cholelithiasis. Ann Surg 1991, 213: 605-77.
7. Peters JH, Ellison EC, innes JT, et at, Safety and efficacy of Laparoscopic Cholecystectomy. A prospective analysis of 100 initial patients. Ann Sugr 1991; 213: 3-12.
8. Cunninghan AJ, Brull SJ. Laparoscopic Cholecystectomy Anaeth. Analg 1993; 76: 1120-1133.
9. Lui, Sy, Leighton T, Davis I, et al. Prospective analysis of cardiopulmonary responses to Laparo scopic chlecystectomy.
10. Odebery S, Ljurqvist J, Svenburg T, et al Haemodynamic effects of Pneumoperitoneum and the influence of Posture during anaesthesia for Laparoscopic surgery. Acta. Anaesth. Scand 1994; 38: 276-283.
11. National Institute of Health consensus development conference statement on gallstones and Laparoscopic Cholecystectomy. Ann. J. Surg. 1993; 165: 390-398.
12. Super NJ, Dunnegan DI, Laparoscopic Cholecystectomy. Experience of a single surgeon. World J. Surg 1993, 17: 16-21.
13. Dubios F, Icard, Berthelot G, Levard H, Cocliscopic Cholecystectomy. Ann Surg. 1990, 211: 60-62.
14. Holzman M, Sharp K, Richarrds W, Hypercarbia during Co_2 gas insufflation for caution. Surg. Laparoso Endoscopi 1992, 2: 11-14.
15. Wolfe BM, Gardiner BN, Leary BF, Frey CF. Endoscopic cholecystectomy An analysis of complications. Arch. Surg. 1991, 126:11[illegible] 1198.
16. WIttgen CM, Andrus CH, Filzgerald SD, DL, Analysis of the haemodynamic and ventilatory effects of Laparoscopic cholecystectomy. Arch Surg. 1991; 126: 997-1001.
17. Marshal, RL, Febson JR, Davie T, et al circulatory effects of Co_2 insufflation of the peritoneal cavity Laparoscopy. J. Reprod Med 1981, 26: 338-46.
18. EL. Minawi M, Wahbi O, EL, Bagoun I, Sharawi M, EL. Mallah S. Physiologic changes during Co_2 No Pneumoperitoneum in diagnostic Laparoscopy. J. Reprod Med. 1981; 26: 338-456.
19. Yoris, JL, Noirot, DP, Legrand MJ, et al. Hemodynamic changes during Laparoscopic cholecystecomy. Anaesth - Analog 1993, 76: 1067-71.
20. Smith L, Benze, RJ, Nanethe, LM et al, Cardiovascular effects of peritoneal insufflation of Co_2 for Laparoscopy, Br. Med. J. 1971, 3: 410-411.
21. Invankovich AD, Miletich DJ, Albrecht RF, et al Cardiovascular effect of intra peritoneal insufflation with Co_2 in dogs. Anaesthesiology, 1975; 42: 281.
22. Kelman GR, Kamegis YN, Palterson RP, et al, Cardiac output and arterial blood gas tension during Laparoscopy. Br. J. Anaes 1972, 44: 1155.
23. Motew M, Invankovich AD, Biengiarz J, et al Cariovascular effects and acid base and blood gas changes during Laparoscopy. Ann. J. Obstct Gyneacol> 1973, 115: 1002-1012.
24. Leniz RJ, Thomas TA, Wilkins DC, Cardiovascular changes during Laparoscopy studies of stroke volume and cardiac output during impedance cardiography. Anaesthesia 1976, 31:4.

EARLY DIAGNOSIS OF NEONATAL SEPTICEMIA

Charoo B.A. D.Ch, M.D.; Muzaffar Jan D.Ch., M.D.; Mushtaq Ahmad M.D.; Wajid Ali M.D.; Masood-ul-Hassan M.D.; A.S. Sethi M.D.

Abstract: *Neonatal bacterial infection continues to be one of the major causes of morbidity and mortality in developing countries. It accounts for about half of all neonatal deaths in India. Early diagnosis and prompt therapy results in a much better outcome than if a delay in diagnosis is made and the therapy delayed thereof.*

This study evaluated 50 newborns admitted with clinical diagnosis of septicemia and 20 controls and was carried out in the neonatal section of the children's Hospital at Srinagar. The study compared the results of rapidly available diagnostic tests with those of blood culture. The study provides information on the value of several simple and cheap laboratory tests used singly and in combination. The test results were available in one hour and could decide the choice of therapy.

Neonatal sepsis is a fairly common problem seen in our nurseries. Outcome of neonatal bacterial infection is directly proportional to the time spent in diagnosing and therefore the start in therapy. Since symptoms and signs stimulate most of the disorders in this age group; like hyperglycemia, intracranial bleed; Birth anoxia, it becomes very difficult to differentiate these conditions from neonatal sepsis on clinical grounds alone; likewise a large number of patients who have disorders other than neonatal sepsis are put on antibiotics unnecessarily. It is therefore mandatory to develop ways and methods which would result in early detection of infection and institution of a rational therapy.

Key words: *Septicemia, Band cell count, Micro ESR, C-reactive protien.*

JK-Practitioner 1999; 6(3): 218-219

Materials and Methods:

50 sick neonatals admitted in the neonatal section of the Childrens Hospital, Srinagar, from January 1992 to April 1993 with the strong clinical suspicion of septicemia were taken up for study. A detailed history of perinatal events was obtained in each neonate and a detailed physical examination was done.

About 20 neonates attending the immunization clinic of the same hospital served as controls. The babies selected were those presenting with clinical features of lethargy, refusal to feed, vomiting, diarrhoea, respiratory distress, convulsions, jaundice and temperature instability. Hematological parametres were done on blood obtained by deep heel prick.

Total white cell counts were done in Neubaur chamber after staining with leishman stain.

Different counts were done under oil immersion lens. From the percentage of each cell type the absolute number of neutrophils and band forms per cubic millimeter were calculated. For determining micro ESR micro hematocrit tubes were filled completely with blood drawn by capillary action. One end of the tube was closed with wax and the tube was fixed vertically by means of sticking plaster. The fall in erythrocytes was measured in one hour in millimeter.

C-reactive protien estimation was done by latex agglutination method. For blood culture, 2 ml blood was collected under aseptic technique from a peripheral vein and sent for culture and sensitivity.

For gastric aspirate cytology, smears were stained by Leishman's stain and 200 cells were counted. The percentage of polymorphs was then calculated.

All relevant investigations were done wherever indicated.

Results:

Of the 50 newborns suspected of being septicemie, 26 were males and 24 females.

80% of the patients were term whereas 20% were proterm,

Early onset sepsis was seen in 40% and late onset sepsis in 60% cases. Nearly two third of the cases had refusal of feeds as the predominant finding. Respiratory distress was also seen in a higher number of cases. Probably because of bronchopneumonia.

Blood culture was positive in 48% cases. Gram

From the Department of Neonatology (Charoo, Jan, Ahmad, Ali, Prof. Hassan) **SKIMS Soura Srinagar India and the Department of Paediatrics** (Prof. Sethi) GMC Srinagar Kashmir.

Received Jan. 1999 Accepted June 1999

Correspondence to : Dr. B.A.Charoo Senior Resident, Deptt. of Neonatology, SKIMS, Soura, Srinagar-11 Kmr.

negative sepsis was more common Klobsella being the predominant organism (41% of cases) followed by E. Coli (25%).

Total leucocytes and neutrophil counts varried widely in infected and non infected babies and were of little clinical use in the early diagnosis of sepsis.

Band cell count and band cell neutrophil ratio of more than 0.2 were grood parametres in identifying infection.

A band cell/AN/ ratio of 0.2 was present in 62.5% of infected and 69% of probably infected cases.

Positive CRP had the highest sensitivity (80%) and highest (90) respectively.

Among the various combinations, micro ESR and CRP were 66% sensitive and 85% specific and ANC and CRP 75% sensitive and 70% specific.

ANC and CRP was the most sensitive (75%) and Bc/ANC ratio and CRP as the most specific (85%) combination.

Discussion:

Neonatal bacterial infection is a formidable challenge and accounts for nearly half of the deaths in neonatal period in India. Early diagnosis and prompt therapy greatly influence the outcome. The definitive diagnosis depends upon a positive blood culture which may not be avilable evrywhere. Hence the need for safe, simple, rapid and reliable screening tests for early detection of infection. The manifestations of sepsis in the new born are varried and may mimmick many disorders in this period. That is why a battery of tests have been evolved and tried to make the diagnosis in the earliest.

Our study evaluated common hematological tests (viz total and differential counts, band cell counts, micro ESR, CRP) gastric aspirate cytology and compared them with blood culture. The tests were simple and cheap with results available within one hour. There was a fairly well correlation with blood culture positivity and used in combination, the utility of these tests was significant.

References:

1. Bhankee O.N, Aggarwal K.C., Narang Anil and Bhattarjee Santosh, Proqnosis and treatment of neonatal Septicemia-A clinico-bacteriological study of 100 cases. Indian Paediatrics 1974;11:519-528.
2. Boyle Robert J; Chandler Barry D; Stene street Barbara S; and Oh William, Early identification of sepsis in infants with respiratory distress-Paediatrics 1978;61:774-750.
3. Bhandari B; Tak S.K; Gupta R.S.; Ramakrishnan S; Evaluation of a sepsis screen for nonates. Indian Paediatrics 1988;25: 860-863.
4. Chandra A, Rea Nagraj; Srinivas M and Shymala S; Rapid diagnostic tests in neonatal septicemia. Indian journal of paediatrics 1988;55:947-953.
5. Haider S.A; Polymorphonuclear leucocyte count in the diagnosis of infection in the newborn. Archives of disease in childhood 1984;59:435-438.
6. Kalra K; Shyam Sunder; Kalra Ajay; Elhence B.R; DAYAL R.S; Creative protein in neonatal infections. Indian Paediatrics 1985;22:215-219.
7. Kite P; Miller M.D.; Gorhan P; and Cengden P; Comparison of five tests used in diagnosis of neonatal bacteremia. Archieves of disease in childhood. 1988;63:639-634.
8. Namdee U.K; Singh H.P; Rajput V.J.; and Kushwaha J.S.; Haematological indices for early diagnosis of neonatal septicemia. Inian Paediatrics 1985;22:287-292.
9. San Leen; Acute phase proteins for diagnosis and follow up neonatal infections. Indian Journal of Paediatrics; 1986;53:8-9.
10. Sabal K.G. and Wadsworth Ch; C-reative protein in early diagnosis of neonatal Septicemia. Acta Pediatrics Scandinavia; 1979;68:825-831.
11. Singh M. Narang A and Bhakoo O.N. Evaluation of a sepsis screen in the diagnosis of neonatal sepsis. Indian paediatrics 1987;24:39-43.

TESTICULAR LYMPHOMA A HISTOPATHOLOGICAL STUDY OF TWELVE CASES

A.R.Khan M.D.; N.D. Chowdhary M.D.

***Abstract:** Primary testicular lymphomas are rare. An analysis of testicular tumor over a period of 14 years (1984-97) revealed twelve cases of primary testicular lymphomas. Out of a 135 testicular tumors, comprising of 133 primary and two cases of metastatic adeno-carcinoma there were eleven cases of non-Hodgkin's lymphoma and one case of Hodgkin's disease. All the eleven cases of non-Hodkin's lymphoma presented as testicular swelling of 3 weeks to 6 weeks duration. Hodgkin's disease presented with the problem of infertility.*

***Key words:** Testicular tumor, Non-Hodgkin's lymphoma, Hodgkin's disease*

JK-Practitioner 1999; 6(3): 220-222

Introduction:

Primary non-Hodgkin's lymphoma of the testis is defined by a presentation of testicular tumour in the absence of nodal involvement after careful staging[1].

The incidence of clinical malignant lymphoma testis reported in literature varies between 1% to 8% of all primary testicular tumors[2-5]. This is in contrast to microscopic infiltration of 18.6% reported by Civler[6] in 102 males at autopsy in non-Hodgkin's lymphoma.

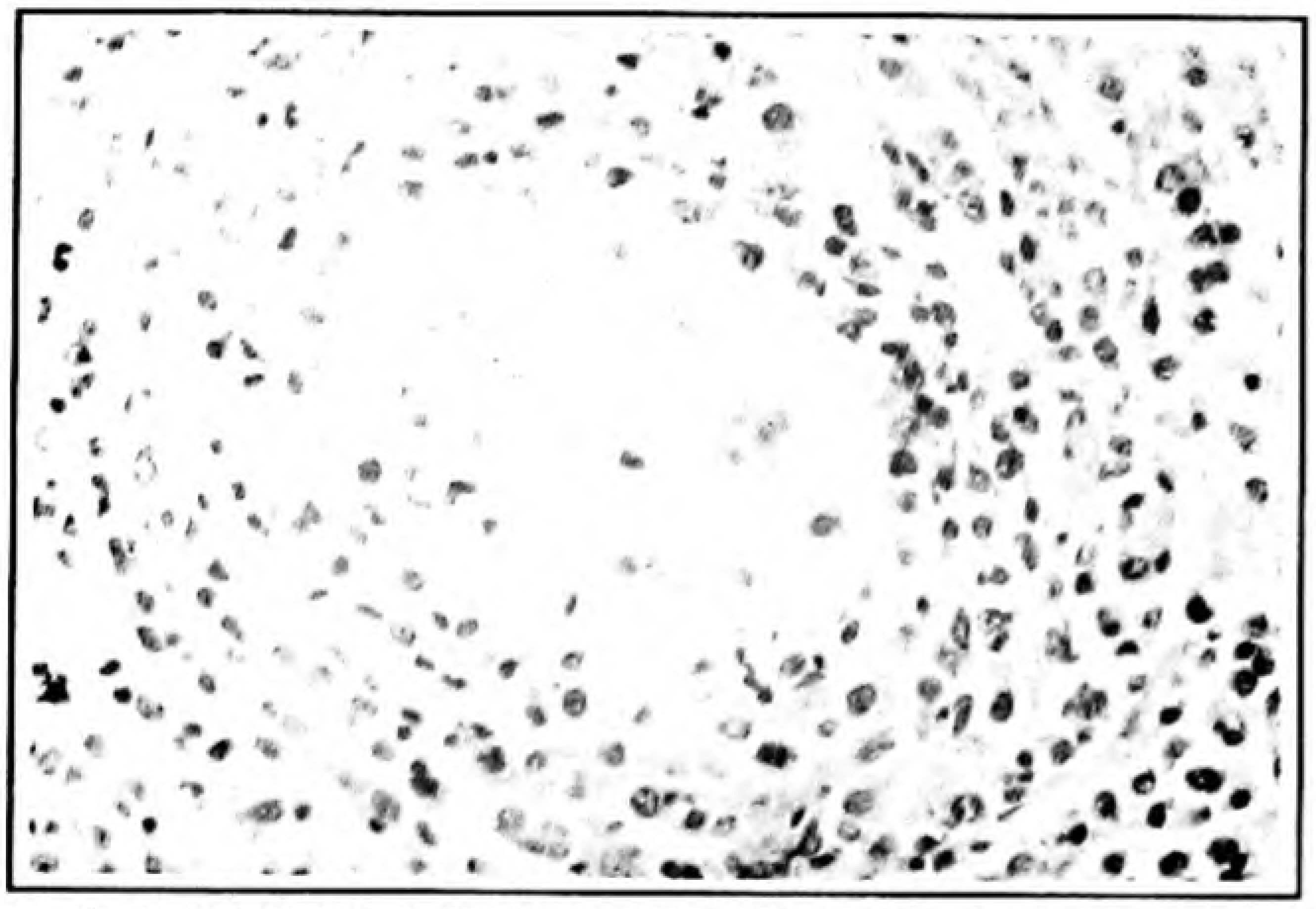


Fig.1 Non-Hodgkin's lymphoma-testes. The lymphoid cells are seen around, a residual seminiferous tubules. HxEx200

Material and Methods:

The present study is based on both retrospective and prospective analysis of testicular lymphomas over 12 years period (1984-95) from the records and material of pathology Department, Government Medical College, Srinagar and referral clinic of one of us (ARK). Material comprised of available sections as well as freshly cut sections from the available specimens and bloks.

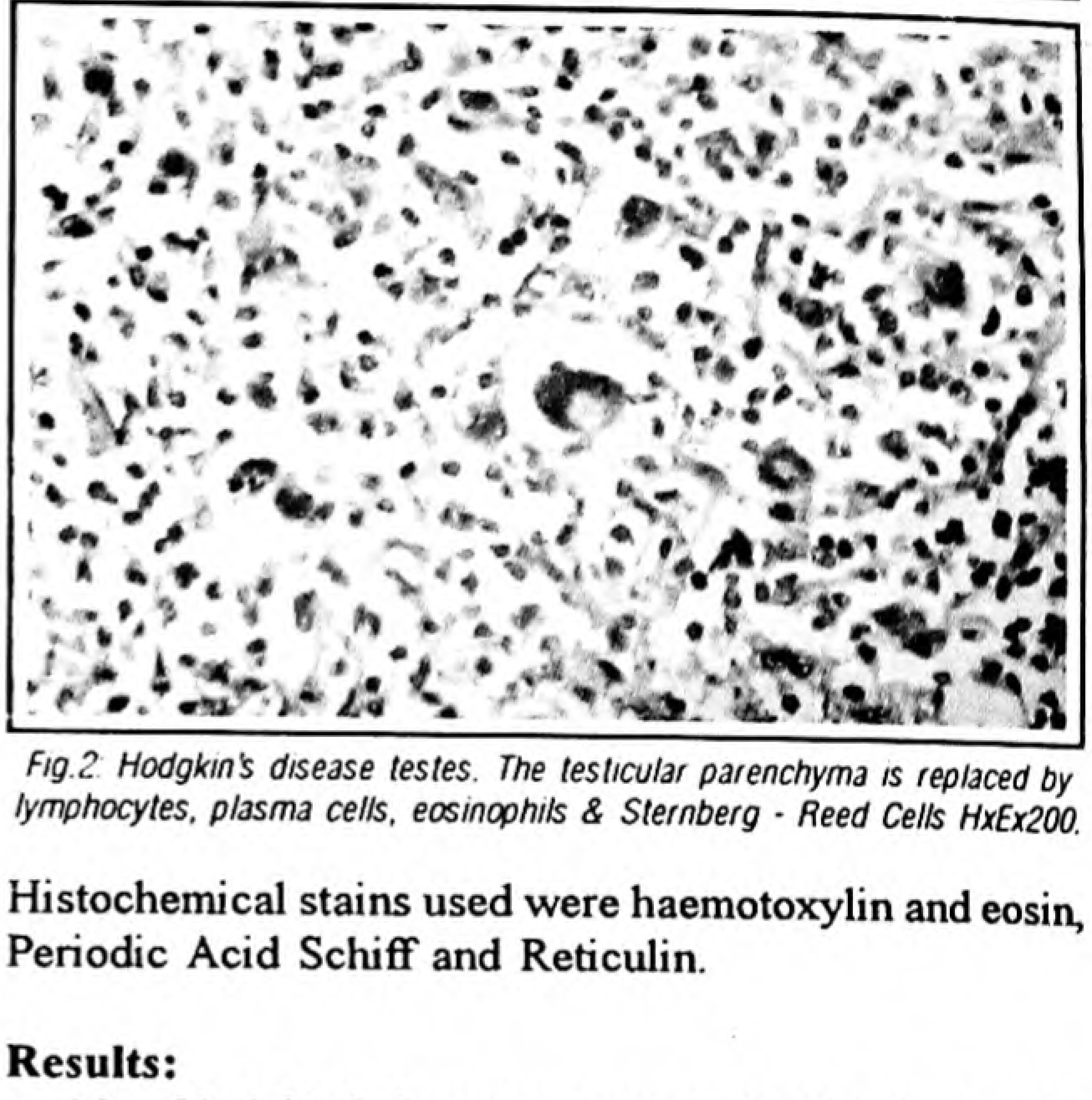


Fig.2 Hodgkin's disease testes. The testicular parenchyma is replaced by lymphocytes, plasma cells, eosinophils & Sternberg - Reed Cells HxEx200.

Histochemical stains used were haemotoxylin and eosin, Periodic Acid Schiff and Reticulin.

Results:

Non-Hodgkin's lymphoma were classified using the working formulation for clinical usage of non-Hodgkin's lymphoma[7]. Rye classification[8] was used for subtyping Hodgkin's disease.

As shown in the table, age of non-Hodgkin's lymphoma varied between 27 years and 85 years. Six out of eleven patients were aged 50 above. The only case of Hodgkin's disease was 25 years old. Right sided involvement was seen in eight and left in four and all the elevan cases of non-Hodgkin's lymphoma presented with testicular swelling of 3-6 weeks duration. Constitutional symptoms were absent in all. However, Hodgkin's disease presented with the complaint of infertility. There were another three cases of non-

From the Department of Pathology Govt. Medical College Srinagar, (Kmr.) (Prof. Khan, Chowdhary)
Received February 1999 Accepted May 1999
Correspondence to : Dr. A.R. Khan, Post Box 298, GPO, Srinagar, 190001, Kashmir, India.

Hodgkin's lymphoma who presented with testicular swelling but were found to have extra-testicular involvement on staging. These were considered as secondary tumors, and therefore, excluded from this series.

Gross

The longest diameter of ten cases of non-Hodgkin's lymphoma varied between 40mm to 80mm. In one case (case No.9) only review slides were available. Three cases had associated hydrocele. Testis was enlarged and distended by tumor with smooth tunica. Outer surface was homogenous and fleshy replacing entire testicular parenchyma. Haemorrhage and necrosis were conspicuous by their absence. In the only case of Hodgkin's disease, testis measure 60mm in longest diameter. Cut section showed entire testis replaced by the tumor with two tumor nodules of 10 mm each on tunica albuginea. Epididymis and cord were free.

Microscopic

Testicular parenchyma in non-Hodgkin's lymphoma showed diffuse lymphoid infiltration with residual seminiferous tubules here and there. The latter showed germ cell atrophy and intratubular lymphoid infiltrate. (Fig.1) Epididymis and cord were infiltrated in two cases. All the eleven cases of non-Hodgkin's lymphoma were categorized as intermediate grade.

The only case of Hodgkin's disease of mixed cellularity sub-type showed entire testicular parenchyma replaced by a diffuse infiltrate including lymphocytes with some eosinophils, neutrophils, plasma cells, histiocytes and dispersed mono-nuclear Hodgkin's cells and multi-nucleated Reed-Sternburg cells. (Fig.2) There was in addition variable degree of fibrosis. The two tumor nodules on tunica albuginea revealed identical histology. Epididymis and cord were free.

Discussion:

Malignant lymphoma of the testis is rare. Our 14 years study revealed a total of twelve cases (9%) out of primary testicular tumors. This includes eleven cases of non-Hodgkin's lymphoma and one case of Hodgkin's disease. We were directly responsible for the diagnosis of five cases of non-Hodgkin's lymphoma and one case of Hodgkin's disease. The remaining three were revised diagnosis by us, reported earlier as Seminoma testis. Our figures are similar to Western figures of 1%-8%[2-5]. The other Indian figures are 4.5% & 1% quoted by Crover et al[9] and Sampat et al[10] respectively. Chitale and Vadera[11] in a 20 years study reported lighteen cases of testicular lymphoma, all metastatic, in a total analysis of 179 testicular tumors.

Malignant lymphoma of the testis is usually seen in old age past sixty[3] compared to mean age of 40 for seminoma and 31 year for teratoma[12]. In a review study of thirty five cases by Turner et al. 23 out of 35 cases were observed in age 50 and above. In our series, six cases (54%) of non-Hodgkin's lymphoma were seen in the age 50 and above.

Clinical involvement of testis by lymphoma in children is rare. This is to be contrasted with microscopic infiltration in lymphoblastic and Burkitt's lymphoma which is not uncommon[6]. Weddel[14] from review of literature found seven cases of testiclar lymphoma in children and added one case of his own. We, in this study, observed one case of bilateral Burkitt's lymphoma in a 5 year old child. But staging revealed the disseminated disease and therefore, not included in primary testicular lymphoma.

All the cases of non-Hodgkin's lymphoma labelled primary by us, were unilateral. Out of three cases of secondary or disseminated lymphomas of the testis and cord, 2 cases showed synchronous bilateral involvement. Therefore, it is inferred that bilateral lymphomas of the testis are secondary lymphomas rather than primary tumours.

Infiltration of the epididymis and cord is more often a feature of lymphoma and leukemia than germ cell tumour. Talerman[16] reported microscopic infiltration of the epididymis in 21 or 27 specimens and cord infiltration in 18 of 26 specimens of non-Hodgkin's lymphoma. Two of our cases showed microscopic infiltration of the cord and epididymis (Refer to table).

All the non-Hodgkin's lymphomas were of diffuse nature. This goes well with what is already reported in the literature[1-7]. All the eight cases of non-Hodgkin's lymphoma cases were catergorised as intermediate lesion. This is in disparity with the clinicopathologic review of Turner et al[13] who in a total of 35 cases of non-Hodgkin's lymphoma found 23 cases in high grade.

Hodgkin's disease of the testis is rare. There are a few reports available in literature namely, those of Sampat et al[16], Hamilton, Kagan and Friedmon[17] and Glaholm, Brada and Horwich[18]. The case reported by us here has not shown any evidence of disease recurrence at 31/2 year follow up. Therefore, it is concluded as primary Hodgkin's disease of the testis.

Differential diagnoses of primary non-Hodgkin's lymphoma testis include granulomatous orchitis, pseudolymphoma and Seminoma. Granulomatous orchitis is characterised by diffuse polymorphous infiltrate with or without giant cells in the interstitium and within the tubules. Pseudolymphoma, is much rare

TABLE:

S.No.	Age (years)	Side (L/R)	Infiltration of Epididymis & cord	Maximum diameter	Microscopic diagnoses
1.	60	R	-	55 mm	Diffuse mixed cell
2.	46	L	-	60 mm	Diffuse mixed cell
3.	40	L	-	62 mm	Diffuse mixed cell
4.	27	R	-	40 mm	Diffuse mixed cell
5.	85	R	Infiltration of cord	68 mm	Diffuse mixed cell
6.	45	R	-do-	60 mm	Diffuse large cell
7.	25	R	2 tumor nodules of 10 mm each on the tunica albuginea	60 mm	Hodgkin's disease mixed cellularity
8.	60	R	-	65 mm	Diffuse mixed cell
9.	34	L	-	(Slides reviewed)	Diffuse large cell
10.	60	R	-	60 mm	Diffuse mixed cell
11.	80	L	-	80 mm	Diffuse mixed cell
12.	50	R	-	58 mm	Diffuse large cell

than lymphoma, characterised by lymphoid follicles with lymphocytes and plasma cells. Seminoma can pose a serious challenge at times. Three cases of this study had been earlier diagnosed as seminoma and another case diagnosed by one of us (ARK) as non-Hodgkin's lymphoma was given the revised diagnosis of Seminoma, at Oncology centre. This patient developed radiation proctitis and one year later non-Hodgkin's lyhmphoma in neck lymph node. Gowing[2] has described morphological features which can be of help to differentiate testicular non-Hodgkin's lymphoma from Seminoma. Other features which support the diagnoses of non-Hodgkin's lymphoma are the short duration and smaller diameter of testicular swelling, more frequent infiltration of the cord and epididymus and absence of insitu germ cell tumour.

Testis like other extranodal sites, namely thyroid and breast does not normally contain lymphoid tissue. Pirmary non-Hodgkin's lymphoma is well recorded at all these sites. Lymphoid tissue may appear in these organs secondary to a clinical or subclinical inflammatory stimulation. Prognosis of genuine primary testicular lymphomas would certainly be better than secondary lymphomas.

References:

1. Paladugu RR, Bearman RM, R Appaport H: Malignant lymphoma with primary manifestation in the gonad: a clinicopathologic study of 38 cases. Cancer 1980;45:561-571.
2. Gowing NFC. Malignant lymphoma of the testis: In Pugh RCB Ed. Pathologyl of testis. London: Blackwell Scientific Publications. 1976; p.134.
3. Kiely JM, Massey BD. Harrison EG. Utz DC. Lymphoma of testis. Cancer 1970; 26:874-852.
4. Mostofi FK. Secondary tumors initially manifest as testicular neoplasms. In Mostofi FK, Price EB, Eds. Tumors of the male genital system. Washington Armed Forces Institution of Pathology, 1973, p.131-136.
5. Pugh RCB. Testicular tumors. Introduction in: Pugh RCB. Ed. Pathology of testis London: Blackwell Scientific Publications 1976; p.139-159.
6. Givler RL. Testicular involvement in leukemia and lymphoma. Cancer, 1959: 32:2390-2395.
7. National Cancer Institute sponsored study of Classifications of non-Hodgkin's lymphomas. Summary and description of working formulation for clinial use. Cancer 1982, 49: 2112-35.
8. Lukes RJ. Craver LF, Hall TC, Rappaport TT, Ruben P, Report of nomenclature committee, Cancer Res. 1966; 16:1311.
9. Grover RK. Kaushal V, Gupta BD. Testicular germ cell tumors. Cancer 1985;56:1251-1256.
10. Sampat MB, Sirsat MV and Kamat MR. Malignant lymphoma of the testis in Indians. Br.J. of Urol 1974; 46:569-575.
11. Chitale A. Vadea V. Neoplasms of testis and paratesticular tissues. In Chitale a Vadera V. Eds. Pathology of Urinary and male genital system. B.I. Churchill Livingstone Pvt. Ltd. 1992;p.228.
12. Dall DC, Weiss RB: Malignant lymphoma of the testicle. Cancer 1972;29:515-524.
13. Turner RR, Colby TV, Mackintosh FR. testicular lymphoma: A clinicopathologic study of 35 cases Cancer 1981, 48: 2095-2102.
14. Waddell RW - Testicular lymphoblastoma in Children, Report of a case and review of the literature, J of Urol 1961, 85:956-959.
15. Johnson DE. Butler JJ- Malignant lymphoma of the testis. In Johnson H.K. Lewis. 1976; 234-248.
16. Talerman A. Primary malignant lymphoma of the testis. The J of Urol 1977; 118: 783-786.
17. Hamilton JA, Kagan AR, Frisdman WB. Lymphomas of the testicle. Cancer 1972;29:1532-1536.
18. Glaholm J, Brada M, Horwich A. J. Royal Soc Med 1989;82:558-559.

MEDULLOBLASTOMAS - A PATHOLOGICAL STUDY

Shah Parveen MD, Shah Azra MD.

Abastract: Eight cases of Medulloblastomas were reported from Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar over a period of 16 years from November 1982 to November 1998. The age of patients ranged between 7 to 16 years. The tumour was seen to be more frequent in males. In seven cases the location was midcerebellar. In one case the tumour was too extensive to determine its origin. Spongioblastic differentiation was seen in one case. Medulloblastomas showed prevelence of 8.75% of the intracranial tumours in children upto the age of 16 years.

Key words: Medulloblastoma, Rosettes, Intracranial Tumour, Neuroblastic, spongioblastic.

JK-Practitioner 1999; 6(3): 223-225

Medulloblastomas are central nervous system tumours that arise from rests of undifferentiated neuroepithelial cells and are located in the cerebellum. They are antenatal in origin and usually come to diagnosis during childhood[1]. These neoplasms are most common of the embryonal tumours[2]. This study presents the histological features and prevalence of medulloblastomas among brain tumours from Sher-i-Kashmir Institute of Medical Sciences, Srinagar.

Material and Methods

The present series consists of eight cases of medulloblastoomas reported from the Pathology Department of the Sher-i-Kashmir Institute of Medical Sciences, Srinagar, over a period of 16 years from November 1982 to November 1998. Details pertaining to age, sex and clinical findings were noted. Fresh tissue obtained from the tumour during surgery was studied by frozen section and the excised surgical specimens were also processed by the routine paraffin embedding method. Four to five micron thick sections were cut and stained by the haematoxylin and eosin and phosphotungstic acid-haematoxylin stains. The microscopic slides were studied in detail.

Results

Prevalence: During the period under study (November 1982 to November 1998) a total of 444 brain tumours were studied out of which 85 were from patients below 16 years of age. There were eight cases of medulloblastomas giving an overall prevalence of 1.80% of all intracranial tumours and 8.75% of all intracranial tumours in children.

Age: The age range was 7 to 16 years, the youngest patient being 7 years old. The other six patients were between 7 to 10 years of age and only one patient was 16 years of age.

Sex: There were six males and two females showing a male preponderance, the male to female ratio being 3:1.

Clinical Findings: Seven cases of medulloblastomas arose in the mid-cerebellar region in the posterior fossa encroaching on the cisterna magna as well as the cavity of the fourth ventricle. In one case the tumour was too extensive to determine its exact site.

Pathology

Gross Examination: The tumours were soft, rather friable. Their cut-surfaces were greyish-white or pink. In one case areas of degeneration and cystic foci were seen.

Microscopic Features: Sections of frozen material as well as the unfrozen paraffin embedded tissue showed a highly cellular neoplasm. Every field was seen to be packed with small round, pear or spindle shaped cells in which the cytoplasm was scanty and poorly defined, the nuclei being round or oval, variable in size (Fig. 1). Mitosis were usually abundant. In three cases neuroblastic differentiation was indicated by the formation of rosettes (Fig.2). In these rosettes the cytoplasm formed carrot-shaped tapering processes with the cell nuclei lying at the periphery, the centre being occupied by the converging processes. Pseudorosettes, around blood vessels (Fig.3) were also seen occasionally. The tumour was supported by a sparse stroma with either neuroglial or connective tissue. In one case

From the Department of Pathology, SKIMS, Soura, Srinagar Kashmir (India) (Shah Parveen, Shah Azra)

Received December 1998 Accepted March 1999

Correspondence to : Dr. Azra Shah, Professor & HOD Pathology & Microbiology, SKIMS, Soura, Srinagar Kmr., GPO 27

spongioblastic differentiation could be witnessed. In this case delicate neuroglial fibrils were demonstrated by phosphotungstic acid haematoxylin stain.

Discussion:

Medulloblastomas are thought to arise from remaining foci of undifferentiated neuroepithelial cells in the region of the medullary velum[4,5]. In normal development these cells migrate to form the external granular layer of the cerebellum[4,6,7,8], which then undergoes further maturation. Under certain circumstances, persistent rests of undifferentiated cells may proliferate to become a medulloblastoma[1].

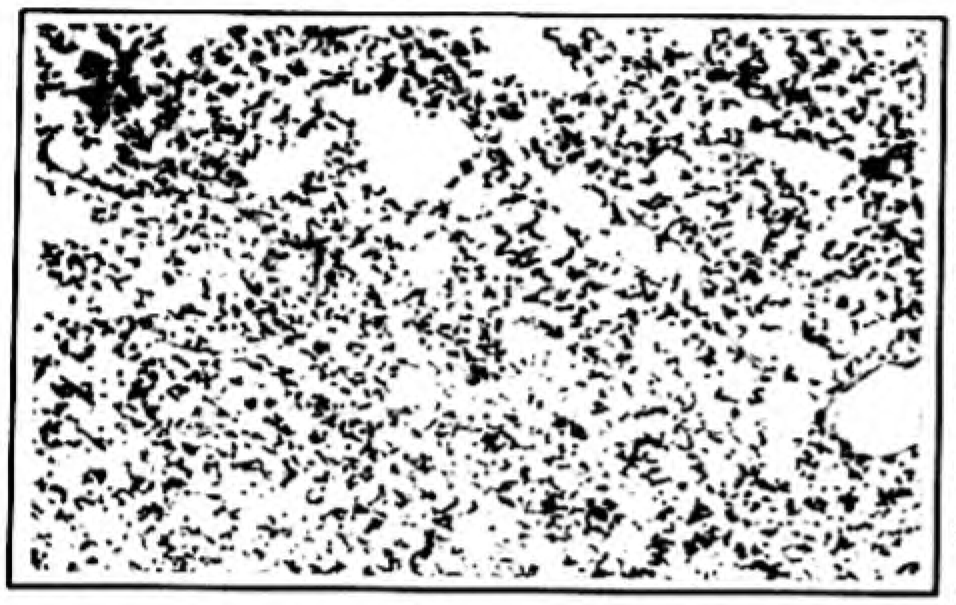


Fig. 1 Photomicrograph showing a highly cellular tumour with sheets of darkry staining, pleomorphic nuclei surrounded by indistinct scanty cytoplasm (HxEx100)

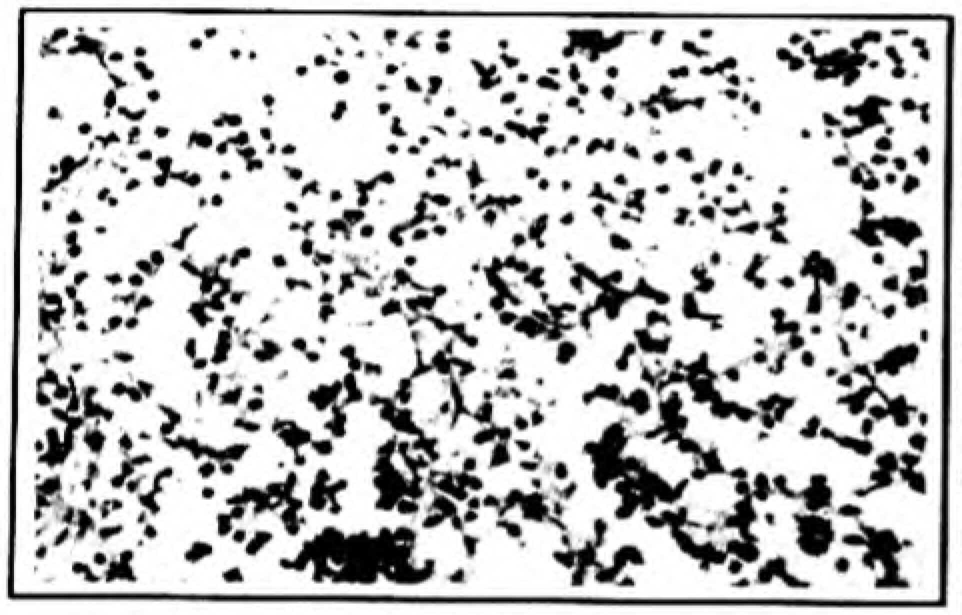


Fig. 2 Photomicrograph showing rosette formation in the centre of the field (HxEx200)

In the present series the prevalence of medulloblastoma is 8.75% of the intracranial tumours of childhood upto age of 16 years. A report from India gives an incidence of 23%[9]. The incidence of medulloblastomas in various other reports has been as 30%, 29% & 24%[10-12]. There is a wide variation in the incidence of Medulloblastomas. Various studies report it as 7 to 20%[13-15].

In our series the age ranged from 7 to 16 years. In view of the antenatal origin of medulloblastomas, and their rapid growth, it is to be expected that the tumours almost always become symptomatic in the first two decades of life[1]. Similar distribution in age was noted by Cushing[16]. The maximum incidence at the end of the first decade has been reported[17]. This is in conformity with our report where the age ranges from 7 to 10 years for all except one of our cases. There was a distinct male preponderance, the male to female ratio being 3:1 as reported earlier[18].

The location of tumours in seven of our cases was midcerebellar. This is the usual location of these tumours especially in childhood[17]. In one of our cases we could not determine the site of the tumour as it was too extensive for the exact site to be determined.

On gross examination the tumours were soft, friable with greysh-white or pink cut-surface. In one case areas of degeneration and cystic foci were observed. These are the usual features seen in these tumours[1,19].

Microscopic examination shows the salient histological features of medulloblastomas with extreme cellularity and areas of neuroblastic differentiation, formation of rosettes, pseudorosettes and rich vasculature. This histological appearance correlates well with other reported series[17]. Medulloblastomas are known to have the capacity of differentiating into several types of cell lines[20]. In one of our cases spongiolbastic differentiation was observed. In this case the neuroglial fibrils were demonstrated by phosphotungstic acid haematoxylin stain, a method which does not stain neurofibrils.

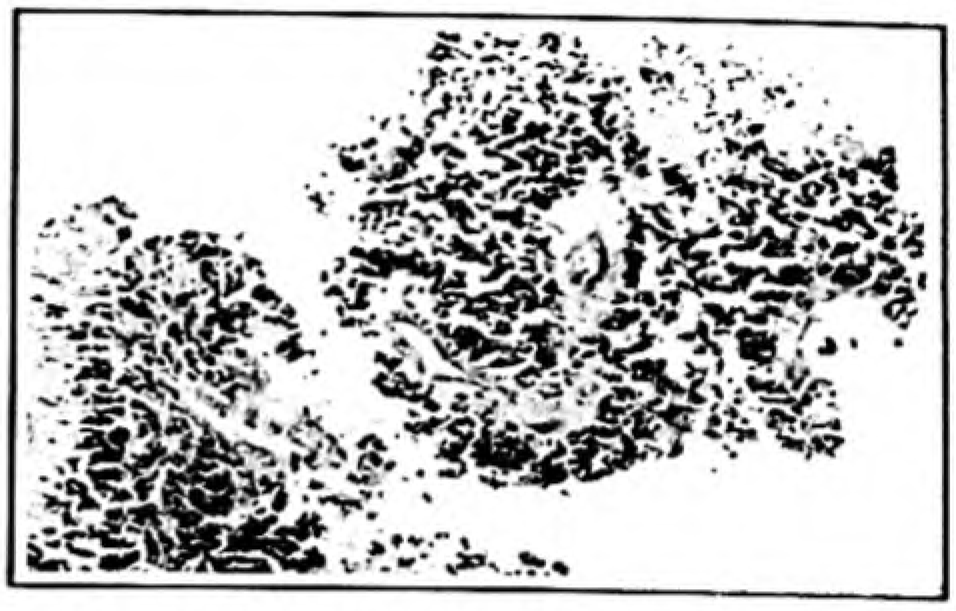


Fig. 1 Photomicrograph showing a blood vessel surrounded by tumour cells forming a pseudorosettee (HxEx100)

References:

1. Farwell JR, Dohrmann GJ, Flannery JT. Medulloblastoma in childhood. An epidemiological study. J Neurosurgery 1984;61:657-664.
2. Juan Rosai, Ackerman's Surgical Pathology Volume II, 7th Edition, 1989. C.V. Mosby Company, pp1713-1778.
3. Milkhorat TH. Paediatric neurosurgery. F.A. Davis Company, Philadelphia, 1978.
4. KadinME, Rubnstein LJ, Nelson JS. Neonatal cerebellar medulloblastoma originating from the fetal external granular layer. J neuropathol Exp Neurol 1970;29:583-600.
5. Rorke LB. The cerebellar medulloblastoma and its relationship to primitive neuroectodermal tumours. J Neuropathol Exp Neurol 1983; 42: 1-15.
6. Rubinstein L. Embryonal central neuroepithelial tumours and their differentiating potential: A cytogenetic view of a complex neuro-oncological problem. J Neurosurg 1985;62:795-805.
7. Rubinstein LJ. Tumours of neuronal cells primitive biopotential precursors: Tumours of the central nervous system (Atlas of Tumor Pathology, 2nd Series, Fascicle 6). Washington, DC, Armed Forces Institute of Pathology 1972; pp130-131.
8. Stevenson L, Echlin F. Nature and origin of some tumours of the cerebellum: Medulloblastoma. Artch Neurol Psychiatry

1934;31: 93-109.

9. Misra BK, Tandon PN, Banerji AK, Bhatia R. Intracranial tumours of infancy, Childhood and adolescence. Ind J Cancer 1984; 21:63-67.
10. Matson DD. Intracranial tumours. Paediatric Neurology. Ed. Th. W. Farmer, Hoeber, New York, 1964.
11. Hooper R. Intracranial and spinal tumours. Tumours of infancy and childhood. Ed. P.G. Jones and P.E. Cambell Blackwell, Scientific Publications, Oxford 1976.
12. Hoffman HJ. Supratentorial brain tumours in children. Neurological surgery Ed. JR. Youmuns, E.B. Saunders Company Philadelphia, 2nd Edition 1982.
13. McGee PG, Isaacson, Wright NA. Oxford Textbook of Pathology, Volume 2b. Oxford University Press 1992; pp1883-1897.
14. Koos WT, Miller MH. Intracranial tumours of infants and children. Stuttgart. George Thieme, 1971; pp205-315.
15. Matson DD. Neurosurgery of infancy and childhood, Ed. 2. Springfield, III. Charles C Thomas 1969; pp448-456.
16. Cushing H. Experiences with the cerebellar medulloblastomas: A critical review. Acta Pathol Microbiol Scand 1930;7:1-86.
17. Russell DS, Rubinstein LJ. Pathology of the nervoous system. Fourth Edition, Edward Arnold 1977; pp146-282.
18. Farwell JR, Doharmann GJ, Flannery JT. Central nervous system tumours in children cancer 1977; 40:3123-3132.
19. Fletcher Christopher DM. Diagnostic histopathology of tumours. Volume 2, 1995 Churchill Livingston pp1161-1219.
20. Kepes, JJ, Morantz RA, Dorzab WE. Cerebellar medulloblastoma in a 73 year old women. J Neurosurgery 1987;21:81-83.

With Best Compliments From

Nira Sons

Chinar Trust Building, Maulana Azad Road, Srinagar-190001

DISTRIBUTORS FOR:

☐ **Hoechst Marion Roussell Ltd.**
☐ **German Remedies Ltd.**
☐ **Fulford India Ltd.**
☐ **S.G. Pharmaceuticals Ltd.**
☐ **Group Pharmaceuticals Ltd.**
☐ **Wockhardt Ltd.**
☐ **Searle India Ltd.**
☐ **Sarabhai Chemicals Ltd.**
☐ **Raptakos, Brett & Co. Ltd.**

ANTI-CANCER DRUGS AND ANTI-RABIES VACCINE AVAILABLE

A STUDY OF FAILURE CASES OF STERILIZATION IN A RURAL AREA OF JAMMU

Chitra Vashnavi M.D.; S.P. Suri M.D.; Vijay Mengi M.D.; Anil Gupta M.S.

Abstract: *2353 women who had undergone laparoligation at C.H.C., R.S. Pura, within a span of five years i.e. 1990 to 1994 were contacted. 21 failure cases were identified from amongst this group. On an average 0.17% of the sterilizations performed every year within this period had failed. Failure was more common among those who had undergone pregnancy associated sterilization being 71.4% (post-abortal) and 14.3% (post-partum). 90.5% of the women accepted some forms of contraception after experiencing failure with the majority (76.2%) opting for sterilization again.*

Key words: *Sterilization failure, Contraception.*

JK-Practitioner 199; 6(3): 226-228

Introduction:

Laparoscopic sterilization is a highly effective method of contraception and this is undoubtedly important to the increasing number of women who are opting for it. The reasons for failure of sterilization are numerous. Pregnancy following sterilization may be the result of conception which had occured prior to the procedure but went unrecognised, spontaneous recanalization of the fallopian tubes, formation of fistulas, or surgical errors.

Objective:- 1) To assess the failure rate of steri lization in a rural set-up.
2) To study the acceptance of contraceptive after failure of sterilization.

Place of Study:- RS Pura Block, Jammu, J&K.

Methodology:- 2353 women who under went sterilization between 1990-1994. (5 years) were contacted personally by the author. Any women who had conceived subsequent to sterilization, irrespective of the fate of the pregnancy i.e. whether terminated or continued, was designated as a 'failure case'.

Observations and Discussions

It was observed that within a period of five years failure rate ranged from 0.51% to 1.48%. The failure rate for five years in the present study was 0.89%. Thus on an average 0.17% of the sterilizations performed in the R.S. Pura block every year between 1990-1994, failed.

ICMR[1] (1982) reported a Nation wide average failure rate for Laparoligation as 0.85%. This is almost similar to the failures encountered for the years 1993-94.

Bhargav and Misra[2] reported a pregnancy rate of 0.97% following sterilization.

Benjamin Al[3] reported failure in 0.53% acceptors after an interval ranging from 6-24 months.

Table-1: Year-wise distribution of failure cases of laparoligation

Year of Laparoligation	Total cases operateu	No. of failure cases	% age failure
1990	337	5	1.48
1991	471	6	1.27
1992	583	3	0.51
1993	548	3	0.54
1994	414	4	0369
1990-1994	2353	21	0.89%

Table-2: Distribution of failure cases as per prior knowledge of possible failure

	Status of awareness	Failure cases	
		No.	% age
1.	Aware	1	4.8
2.	Ignorant/Unaware	20	95.2
	Total	21	100.0

It has been advocated that clients should be given complete, accurate and unbiased information about the available methods of contraception (WHO[4]). Thus, to create an atmosphere of trust between the health care providers and the acceptors, even while advocating sterilization as a permanent method, the small/remote

From the Department of Community Medicine (Vashnavi, Suri, Mengi, Gupta) **Govt. Medical College Jammu (India)**

Received March 1999 Accepted June 1999

Correspondence to : C/o Mr. T.N. Vashnavi, 16 AD, Opp. Police Lines, Gandhinagar, Jammu-180004.

possibility that the method may fail should be communicated to the acceptor, if only to ensure a regular contact with the health personnel.

Table No-2 reflects the awareness of the failure cases about the possibility of the method failing. As many as 95.2% of the failure cases had been absolutely unware about the fact that the procedure might fail while on 4.8% had gained this knowledge prior to the procedure. It, hence appears that there is a definite communication gap between the service providers of all levels and the acceptors of Laparoligation.

Table-3 Distribution of failure cases by time interval between sterilization and conception

Timing of Laparoligation	Failure cases Below 6 mths No.	% age	6 mths-1yr No.	% age	above 1 yr. No.	% age	Total No.	%age
Post-Abortal	9	100.0	3	60.0	3	42.8	15	71.4
Post-Partum	-	-	1	20.0	2	28.6	3	14.3
Interval	-	-	1	20.0	2	28.6	3	14.3
Total	9	100.0	5	100.0	7	100.0	21	100.0
Percentage	42.86		23.81		33.33		100	

Note: Laparoligation was categorised in 3 groups

i) Post-abortal-sterilization done concurrently with MTP or within 6 wks of aseptic induced abortion or spontaneous termination of pregnancy.

ii) Post-partum-sterilization performed within 6 weeks of delivery.

iii) Interval-sterilization performed after 6 wks of abortion/delivery or during any phase of menstrual cycle.

In the present study, 42.8% of the failure cases had conceived within 6 months of undergoing the procedure, while 23.81% had conceived between 6 months to 1 yr and 33.33% after 1 year of the procedure.

Hughes[5] observed that 27% of the failure was were occuring within 6 months, 25% between 6 months to 1 yr and 48% after 1 year.

Mittal[6] et al reported conception in the majority of the failures by 6 months (33.73%), followed by 21.43% who had conceived within 6-12 months and 42.84% after 1 year of surgery. Analysis (Table No.3) of the type of procedure the failure cases had undergone, revealed that the majority of the failures, in the present study, had undergone post-abortal sterilization. Pregnancy associated sterilizations have a greater chance of failing since the fallopian tubes are hypertrophied during pregnancy and subsequent to sterilization and termination of pregnancy undergo involution as a result of which the 'Falope' or silicastic ring may slip.

In 1995, Hazra[7] et al also reported a higher incidence of failures amongst those who had undergone pregnancy associated sterilization (Post-partum/post-abortal).

Thus the women undergoing pregnancy associated sterilization need special care not only during the surgery but also after it as they are at a higher risk of failure. Moreover if an additional effort is made to encourage use of temporary methods till the woman agrees to undergo sterilization and to operate on cases during the early phase of their menstural cycle, the group of women who undergo pregnancy associated sterilizations will decrease and so will the failures.

Table-4: Distribution of failure cases by number of pregnancies following laparoligation

	No. of pregnancies	Failure cases No.	%age
1.	One	19	90.5
2.	Two	2	9.5
	Total	21	100.0

Out of the 21 women whose sterilization had failed, 90.5% had only one pregnancy following sterilization, while 9.5% had 2 pregnancies. No case reported more than 2 pregnancies. Most of the women (90.5%) accepted some form of contraception (table 5) even after experiencing failure. As women with completed families prefer to adopt what for all practical purpose is advocated as permanent method, 76.2% of the failure cases of type study opted for a repeat sterilization (LL) for themselves, while 14.3% accepted CuT. Only 2 cases (9.5%) refused to use any form of contraception at all. These 2 cases had undergone sterilization in the year 1992 and at the time when this study was conducted had already conceived twice each following sterilization.

Table-5: Distribution of failure cases by their choice of contraceptive

	Accepted contraceptive Method	Failure cases No.	%age
1.	Laparoligation (Repeat)	16	76.2
2.	Cu-T	3	14.3
3.	No contraceptive	2	9.5
	Total	21	100.0

It is cases like these, who require special and concentrated efforts of the health workers as well as counselling for adoption of some form of contraception.

Thus women, even after experencing failure after sterilization are willing to reaccept this form of contraception. This reflects the immense popularity of this method. However to ensure that this popularity continues unabated, it is necessary that all aspects of its service provisions should be improved and strengthened, be it the pre & post operative counselling, proper client selection, correct method delivery, or the follow up-services.

Conclusion

1. On an average 0.17% of the procedures performed every year between 1990-94 resulted in failure.
2. Majority of the failure cases (85.7%) had undergone pregnancy associated sterilizations.
3. 95.2% of the acceptors had not been aware of the possibily of failure prior to surgery.
4. 90.5% of the failure cases conceived only once after sterilization as they either accepted sterilization (76.2%) or opted for IUCD (14.3%).

References:

1. ICMR bulletin. "The sequelae of tubal sterilizatin". June 1982; 12: 6.
2. Bhargav Hitesh, Mishra Snehlata. "A long term follow-up study of 923 cases of tubal ligation." Jr. of obstet & Gynae India, 1982;697-701.
3. Benjamin Al. "A longitudinal follow-up of women undergoing Laparoscopic tubal ligation in Ludhiana Block of Punjab." Health and population-Perspectives and issues 1983;8(1):19-28.
4. WHO. "Informing clients about female sterilization." In-female sterilization a guide to provision of services. edition 1992; 47-48.
5. Hughes J.G. "Sterilization failure." BMJ 1977; (1337-1339).
6. Misra Snehlata, Mittal & Dutt Sheela. Survey of sterilization failures Jr. of obstet and Gynae India. Aug. 1982; 3: 555-559.
7. Hazra Maya, Kumari Beena, Maitra Nandita. "Pregnancy after tubal ligation." Jr. of obstet and Gynae, Indian 1995; 45: No.3.

With Best
Compliments From

KASHMIR PHYSIOTHERAPHY
&
REHABILITATION CENTRE

HRDC CAMPUS, POST OFFICE LANE, RAJBAGH, SRINAGAR-8
TELE : 450920

CRANIAL HYPEROSTOSIS

Syed Raffi, M.D.; Tanveer Mir, M.D., F.A.C.P.

Abstract: *A case of Senile Calvarial Hyperostosis, a condition known since ancient times yet poorly understood has been described. It is known to be a variant of Hyperostosis frontalis interna and characterized by marked thickening of skull particularly the inner surface of the frontal bone. This patient presented with memory loss, forgetfulness, inappropriate answers over a few months. Dementia work up did not reveal any reversible causes. No co-morbidity like obesity, virilism, hyperprolactinemia, hypothyroidism were found to be associated. This is a case of Senile Calvarial Hyperostosis of unknown etiology deserved to be recognized in evaluation elderly patients. However its relationship with dementia has not been determined.*

Keywords: *Cranial Hyperostosis, Senile*

JK-Practitioner 1999; 6(3): 229-231

Miss L, an eighty-two year old white female was admitted to geriatric floor with the diagnosis of urinary tract infection. An initial evaluation indicated that she had symptoms suggestive of dementia in the form of memory loss, confabulation and jargon speech. On questioning her: "Ms. L. How are you today?", She answered appropriately," I am fine, thank you." However she was not oriented to time and place. When she was asked, Can you tell us who is the president now?. She replied:". Why, George Bush. Go away". Her remote memory was intact. She was able to tell her mother's maiden name. She was also able to repeat the sentence told to her, suggesting that her immediate memory was intact. She was having some short-term memory loss and confusion.

To test her abstract reasoning we asked her, Can you explain the meaning of : " A bird in hand is worth two in bush"?. She answered, " Two birds are good for you. Don't bother me". We initiated a dementia work up to look for a reversible cause. All tests including SMA-12, B-12, Folate, VDRL, CSF studies were negative. CT scan done as part of initial work up revealed marked thickening of the inner table of skull almost to the extent it seemed to compress the brain. (Fig:1). However the bone scan was normal. The hormonal studies revealed no endocrine etiology. Finally a bone biopsy was performed to rule out metastatic disease which revealed nothing but normal skull bone. (Fig:2). Patient completed her therapy and was discharged to the nursing home. We conclude this picture is suggestive of Senile Calvarial hyperostosis, a variant of Hyperostosis frontalis interna.

Introduction:

Hyperostosis frontalis interna (HFI) is the name generally applied to skull thickening more or less restricted to the squamous portion of the frontal bone and involving in particular its subdural surface or inner surface. This condition is almost observed exclusively in females, irrespective of the attendant circumstances under which it is encountered.[1]

Hyperostosis of the skull has been a well reported entity since the year 300 AD from a cemetery in Nubia, Sudan. The association of this calvarial thickening with virilism and obesity is a clinico-anatomic complex referred to as the Morgagni syndrome or Stewart-Morel syndrome.[2] Hyperostosis frontalis interna is the central feature of a syndrome first described over 2000 years ago by the early pathologist Giovanni Battistta Morgagni, professor of anatomy at Padua (1719). He found the thickening of the inner tables of the frontal bones in obese and elderly women. Stewart(1928) and Morel (1929) independently added the neuropsychiatric problems to this complex and questioned the possibility of an endocrine basis for this syndrome.[2]

Incidence:

Hyperostosis frontalis interna (HFI) is a common, often incidental finding on a CT Scan. It is reported to occur most frequently in females. A female to male ratio of 9:1 has been quoted[3]. 15-20% of women in the 40 to 60 year age group are reported to have evidence of HFI. James D. Fulton et al[3] noted 72% of patients with acromegaly had the evidence of HFI on skull x-ray.

From the Department of Medicine, Nassau County Medical Centre, East Meadow NY (Syed, Mir)

Received April 1999 Accepted June 1999

Correspondece to : Nassau County Medical Center, Department of Internal Medicine, 2201 Hempstead Turnpike East Meadow NY 11554

However female : male ratio in acromegalic HFI was 1.6:1. This suggests a possible endocrine etiology of HFI in some cases.

There are also a few case reports where transmission in the autosomal dominant fashion has been reported.[4]

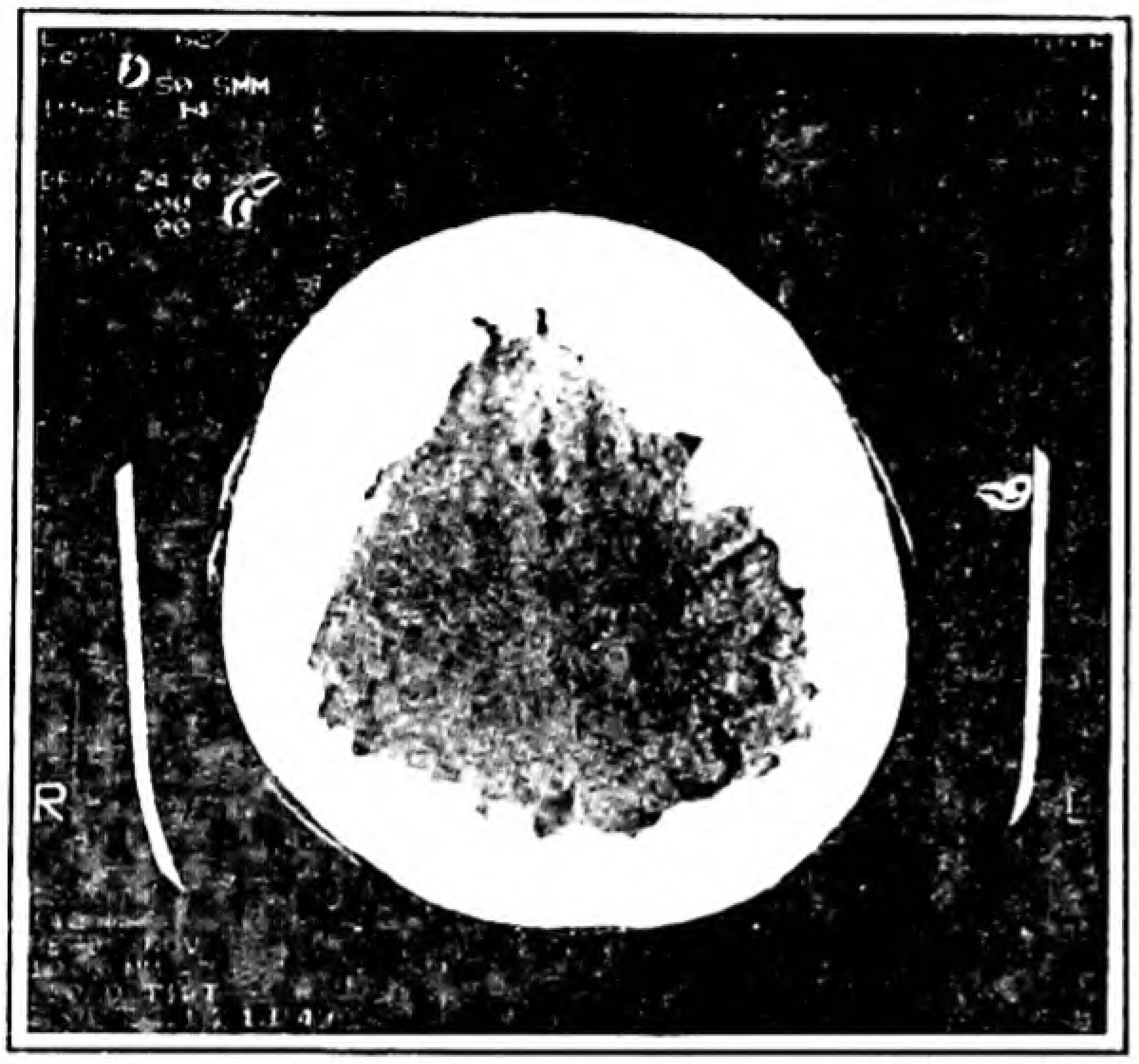


Figure 1:
CT scan of brain without contrast showing diffuse hyperostosis of the skull. This was noted as an incidental finding.

Pathology:

On anatomic examination, the dura is even more intimately adherent to the thickened portion of the frontal bone than it would normally be. Architecturally the thickened region may show the normal proportion of diploic bone to tables is excessive. Either both of the tables may be even abnormally thin. Not uncommonly the diploic bone is dense and sclerotic. The calvarial thickening results from the deposition by the dura of new bone on the inner table. Concomitantly, however this table tends to undergo spongification from the diploic side. For this reason, it is largely diploic bone that is excessive in the thickened portion of the calvarium. At autopsy in a case in which the hyperostotic squama frontalis presents one or more large knobby thickenings on its inner surface, it is not unusual for finding the immediately underlying frontal part of the brain depressed.

Associated conditions:

Stewart and Morel found the presence of hyperostosis frontalis interna in women who were insane, obese and had insomnia and nocturnal restlessness. They also noted polyphagia, polydipsia, urinary disturbances, equilbrium disturbances, visual disturbances, headaches and

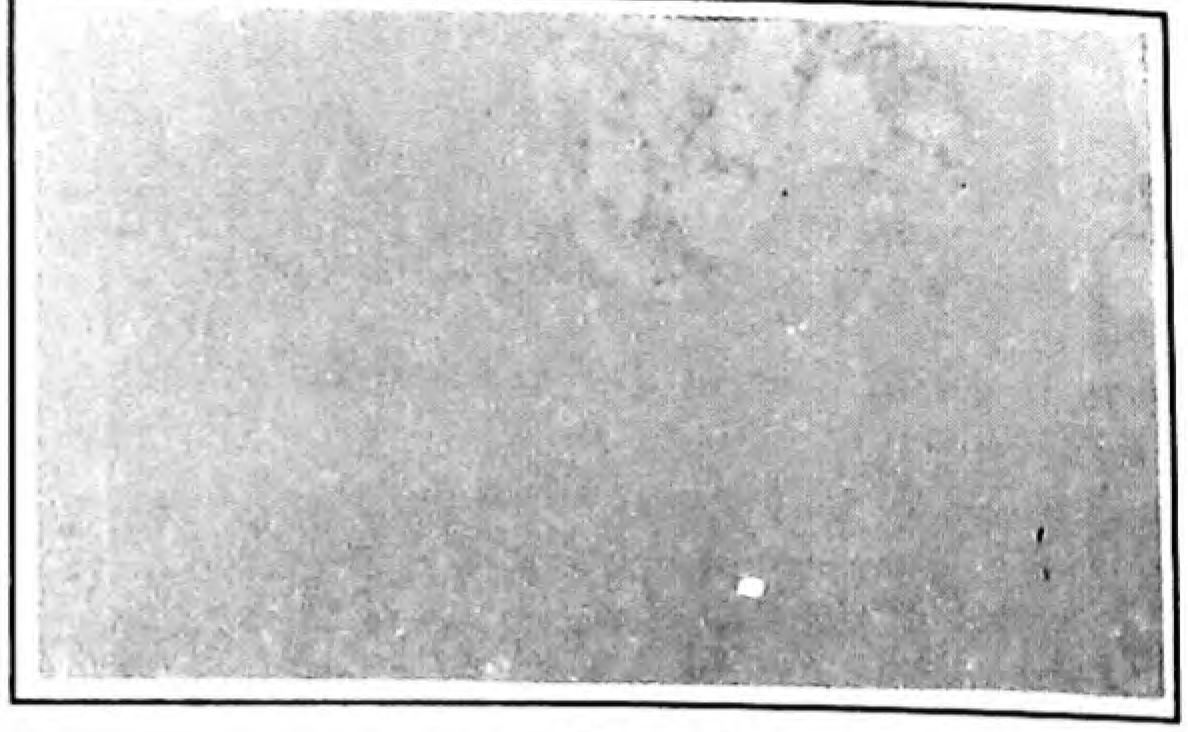


Figure 2:
photomicrograph of the skull bone showing demineralized bone tissue and normally appearing marrow fragments in hematoxylin and eosin.

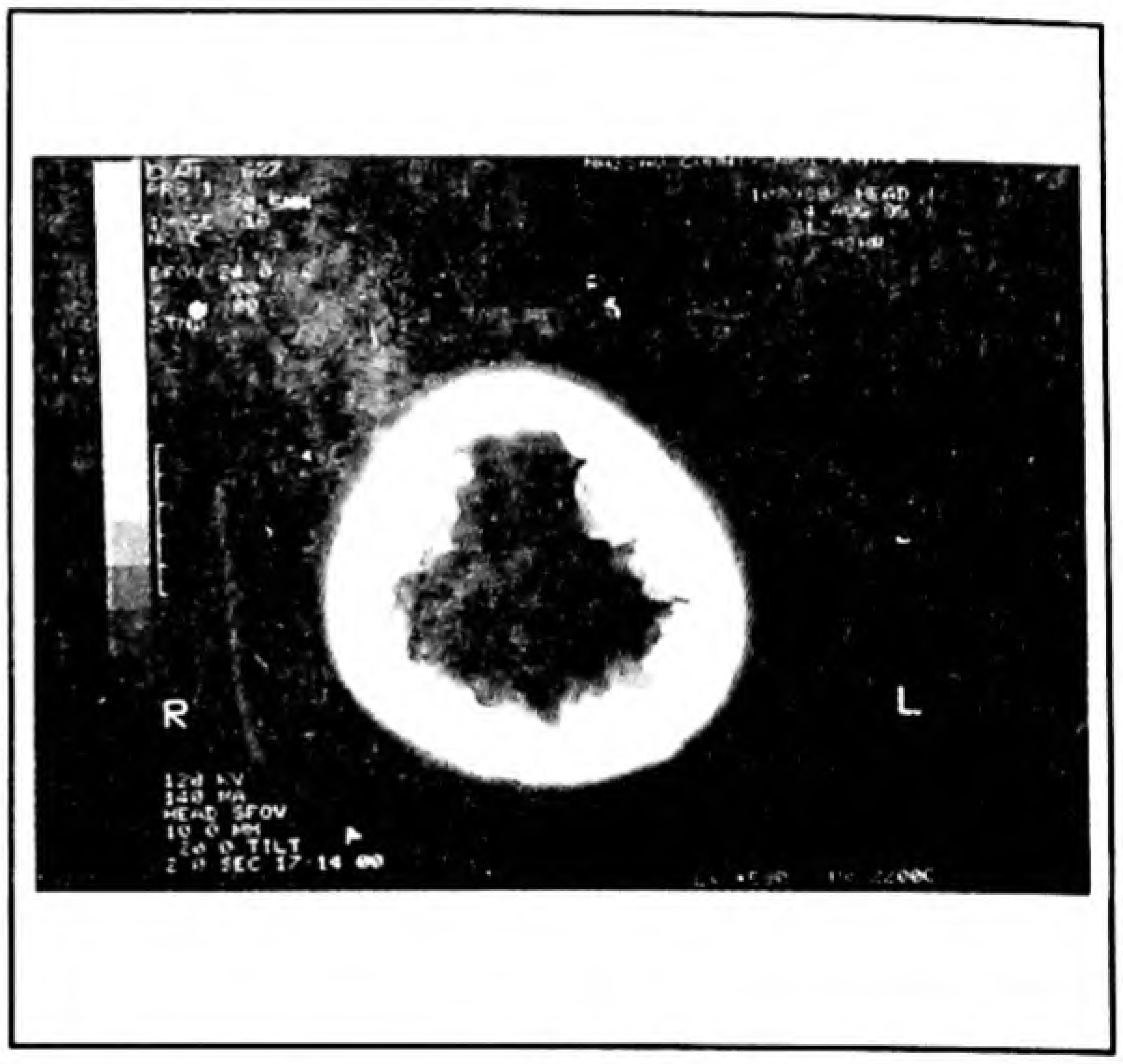


Figure 3:
CT scan picture of the bony window. Note the markedly widened diploic space and the thickened and irregular inner table.

convulsions. These findings were integrated into one as internal frontal hyperostosis with adiposity and cerebral difficulties. Some authors suggest that the formation of endocranial exostoses in these patients is to a certain extent independent of the development of other clinical symptoms, including psychopathological ones, and that the latter are nonspecific for the above syndrome.[5] The cause of HFI remains unknown but appears to be strongly associated with acromegaly, particularly in the presence of co-existent hyperprolactinemia.[3,6] In acromegaly, also there may be thickening of the frontal and parietal bones from new depositions on their inner surface by the dura. The associated involvement of the mandible in acromegaly is so characteristic, however, that confusion with the Morgagni syndrome is again not likely to arise. The other associated conditions described with HFI are hypoparathyroidism, and renal osteodystrophy (Uremic leontosis).[7,8] Not to be forgotten is that HFI may occur due to secondary changes due to the metastases of a lobular carcinoma of the breast.[9]

Radiographic features:

Roentgenographic examination of the part of the frontal bone involved in the hyperostosis is found abnormally radioopaque. (Fig:3). The contour of the inner surface of the thickened part of the bone usually appears irregularly ridged, knobby, and bumpy instead of smooth.. The contour of the outer surface of the affected bone is not altered anywhere.

Senile Calvarial Hyperostosis:

Here the calvarial thickening is generalized. The process of its development is essentially that of new bone deposition on the inner table by the dura and progressive diploization of this table. However, the normal proportions between the tables and the diploic bone tend to be retained in senile calvarial hyperostosis, though the diploic bone may be rather densified because of thickening of its trabeculae. This diffuse form of hyperostosis is observed more often in females than in males. It probably represents an attempt at accommodation to senile brain shrinkage. Diffuse calvarial thickening is also commonly found in connection with general paresis and senile and epileptic dementia. In these conditions it apparently has the same cause and the same manner of development as it has in senile persons without dementia.

Treatment:

An effort must be made to determine the cause. If no cause could be found treatment remains symptomatic. A case of Hyperostosis frontalis interna with severe headaches has been reported and required surgical removal of the frontal bone and the dura.[10]

References:

1. Jaffe, Henry L. Metabolic, Degenerative and Inflammatory Disease of Bones and Joints. Chapter II: 272-275:Lea and Febiger. Philadelphia 1972.
2. Armelagos GJ, Chrisman OD. Hyperostosis frontalis interna: a Nubian case: The American Journal of Physical Anthropology. 1988. 76(1): 25-8
3. Fulton JD. Shand J. Ritchie D. McGhee. J. Hyperostosis frontalis interna, acromegaly and hyperprolactinemia: PostGraduate Medical Journal 1990 .66(771):16-9.
4. Manni JJ, Scaff JJ, Huygen PL, Cruysberg JR, Vergagen WI. Hyperostosis cranialis interna; a new syndrome with autosomal dominant inheritance: Nederlands Tijdschrift voor Geneeskunde. 1990,.134(35):1697-701,
5. Bakhur BT, Bondar AM, Chekler LA, Starodubtseva GK. Clinical picture and genesis of neurophyschiatric disorders in the Morgagni-Stewart-Morel syndrome. Zhurnal Nevroptaologii i Psikhiatrii Imeni S-S- Korsakova. 1987.87(6):911-4,
6. Pawlikowski M. Komorowiski JM. Hyperostosis frontalis and prolactin secretion. Experimental and Clinical Endocrinology. 1987. 89(1):109-11
7. Nakamnishi MS, Neshige R, Kuroda Y, Inoue Y Rinsho Shinkgeigaku. Clinical Neurology. 1990 .30(10):1114-7.
8. Lee VS, Webb MS Jr, Martinez S, McKay CP, Leight GS Jr. Uremic leontosis ossea.:"Big-head" disease in humans? Radiologic, clinical, and pathologic features.Radiology 1996 233-40,
9. Prescher A., Adler CP. Anatomischer Anzeiger. 1993. 175(6):553-9
10. Radek A, Piwowarski W, Machiejckzak A. A case of Morgagni-Morel-Stewart syndrome with violent headaches predominant in the clinical course treated surgically. Neurologia i Neurochirurgia Polska. 1995 29(2):253-6.

VON-HIPPEL-LINDAU DISEASE

Madhu Gupta M.D.; R.C. Nargotra M.D.; Sunita Malhotra M.D.; Shabir A. Bhat M.B.B.S.

Abstract: *Von-Hippel-Lindau Disease is a rare disorder involving multiple organs. This complex angiodysplasia consists of association of retinal capillary angioblastomas with multiple Hemangioblastomas of brain and spinal cord. Angiomas and Cysts of liver, pancreas kidneys are known to occur. This case is presented because of its uncommon nature and interesting CT findings.*

Key words: *Von-Hippel Lindau Disease; Angiodysplasia, Cyst.*

JK-Practitioner 1999;6(3): 232-233

Case Report:

A 28 year old woman presented with history of headache, ataxia and gradual loss of vision, complete loss of vision in left eye 5 years back. She was diagnosed as a case of Angiomatosis Retinae out side our institution. Physical examination revealed thin built female unable to walk properly. Clinical examination did not reveal any neurological deficit. B.P. was 150/100 mm of Hg. Investigations revealed Hb of 12 ogm. Renal and liver functions were normal. Eye examination revealed no light perception in left eye. Slit lamp examination, revealed normal anterior segment of right eye. Fundus examination with indirect opthalomoscopy revealed fibrovascular proliferation and angiomas on the posterior pole in right eye.

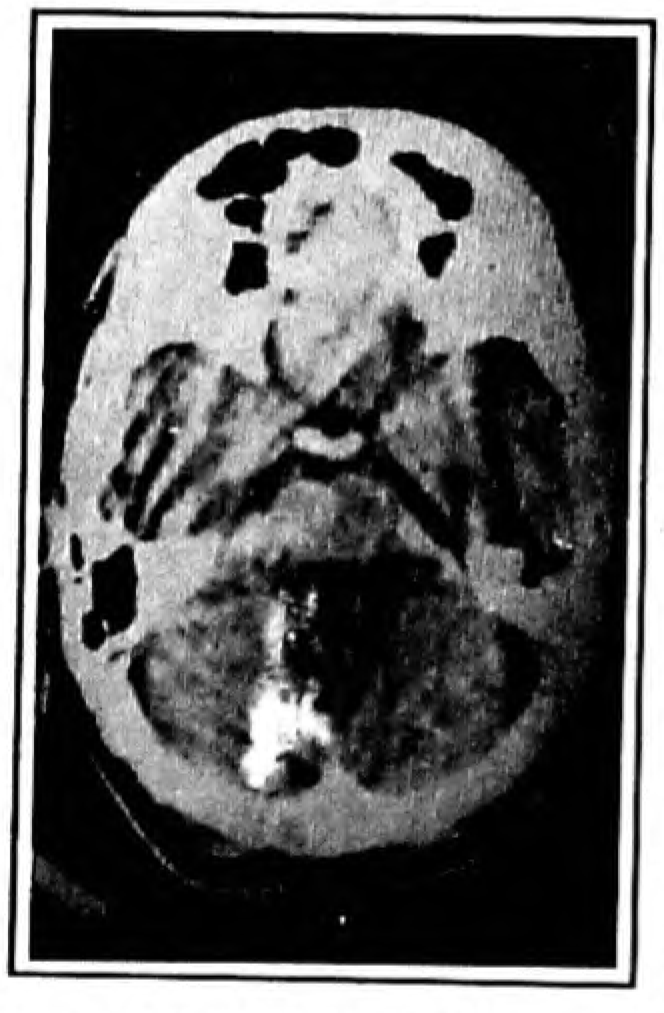


Fig.1: Contrast CT Scan Showing Hypodense mass in Vermis of Cerebellum with opacified nodule in left cerebellum.

To evaluate ataxia, both plain and contrast CT Scan of Head was obtained. Plain CT Scan revealed a large, well Circumscribed oblong, Hypodense mass (A-v 19) in the vermis of cerebellum with moderate obstructive Hydrocephalus. Contrast CT Scan showed marginal enhancement of cyst reflecting compressed cerebellum along with Homogenously Opacified nodule in the leftcerebellum. Diagnosis of Cerebellar Hemangioblastoma was made (Fig.1,2).

Real time US of abdomen was done to rule out any other lesion. US of abdomen showed multiple cysts of variable size in left lobe of liver. Cysts were also seen at upper pole of right Kidney. Left Kidney, adrenals and pancreas were normal.

Discussion:

Von Hippel Lindau Disease is transmitted as an autosomal dominent disorder (encoded on chromosome 3) but many cases are sporadic. Some cases are familial. In patients of Von Hippel Liudau disease there is a high incidence of multisystem manifestations including retinal angiomas, cerebellar and spinal cord angiomas, renal, pancreatic or epididymal cysts, renal cell carcinoma, Erythrocythemia and Pheochromocytoma[1,2].

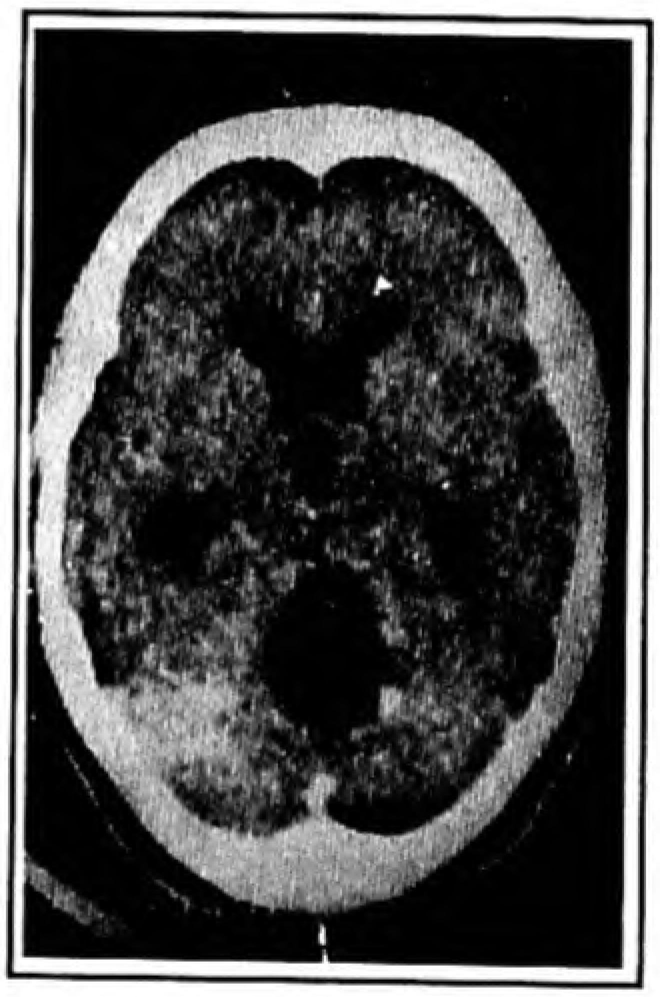


Fig.2: CT Scan Showing moderate obstructive Hydrocephalus.

The average age of onset of neurologic findings in patients with hemanogioblastoma is middle to late thirties, but patients of VHL disease present early[3]. Hemangioblastomas usually involve cerebellum as cystic tumour with a small vascular mural nodule. Multiple tumours are found approximately in 10% of cases[1] CT is now accepted as initial neuroradiological procedure in evaluation of a suspected posterior fossa tumour[3]. The most typical CT feature is a low density cyst, with A.V. only slightly higher than that of CSF. Contrast enhancement Classically produces intense

From the Department of Radiology Govt. Medical College, J&K State India. (Gupta, Nargotra, Malhotra, Bhat)
Received April 1998 Accepted March 1999
Correspondece to : Dr. Madhu Gupta, Q.No: 21, Sarwal Colony Jammu - 180005.

increase in CT density of margin of the cyst but vascular component in form of a mural nodule. Occasionally small nodule is present unaccompanied by a Cyst and less commonly a large solid tumour may have no cystic component. CT has replaced vertebral angiography as the procedure of choice in identifying and localizing hemangio bastomas. In few cases angiography may still be necessary to demonstrate nodule. The present case is a rare association of haemangioblastoma, retinal angiomas with Cysts in Liver and Right Kidney. Retinal angiomas resulted in gradual blindness while hemangioblastoma resulted in headache and ataxia. Ultrasonography helped to diagnose cysts in the liver and right kidney.

References:

1. Melmon KL, Rosen SW, Lindau's disease Review of Literature and study of a large kidney Am. J. Med. 1964; 36: 595-617.
2. Lee DR, Wulfs berg E, Kepes JJ: Radiological aspect of Kidney in Hippel-Lindau syndrome: Radiology 1977; 122:649-655.
3. CT and Angiographic evaluation of Hemangioblastoma Radiology 1981;138:65-73.

SUBSCRIBE

Subscription Rates (India) in Rupees

	1 yr.	3 yrs.
Personal Rate	400	1000
Standard Rate	500	1200
Reduced Rate	250	x
Life Membership	**3000**	**10 Yrs**

Standard rate is for Institutions and Libraries
Reduced rate is for undergraduate students, interns and those under-going post graduate courses

Foreign

	1 yr.	3 yrs.
Gulf Countries	100 SR	275 SR
Rest of the World	$US 100	$US 200

JK-PRACTITIONER The International Journal of Current Medical Science & Practice

Name ____________________

Address ____________________

____

Institution/Hospital ____________________

Please tick box

☐ Yes send me JK-Practitioner

☐ Personal ☐ Standard ☐ Reduced

☐ I enclose a cheque/bank draft payable to the editor, JK Practitioner at Srinagar. (SBI, JK Bank or Grindlays Bank)

Expiry date ____________________

Signature ____________________

Date ____________________

Please return this order form to Dr. G.M. Malik, P.O.Box 884 GPO
Srinagar 190 001 (Kashmir)

ANAPLASTIC MYELOMA--A REPORT OF TWO CASES

Geetha N, M.D.; Nileena N, M.D.; Beela Sarah Mathew, M.D.; Koilparampil T, M.D.; Lali V.S. M.B.B.S.; Rajan B, M.D.

Abstract: *Anaplastic myeloma is an uncommon variant of multiple myeloma which represents only 3.3% of all patients with myeloma. It has different clinical and morphologic features. We describe 2 patients with anaplastic myeloma. One patient received combination chemotherapy and was alive for 6 months.*

Key words: *Anaplastic myeloma, Blast cells.*

JK-Practitioner 1999; 6(3): 234-235

Introduction:

Multiple myeloma represents a malignant plasma cell disorder that accounts for 1% of all haematopoietic disorders[1]. The clinical picture in myeloma depends on bone marrow infiltration by plasma cells or an abnormal paraprotein production. Like any other B cell lymphoproliferative disorder, multiple myeloma may also show an immature picture morphologically and behave more aggressive clinically. Anaplastic myeolma is an unusual variety of multiple myeloma which is characterised by different clinical and morphological features from typical multiple myeloma and plasmacytoma. It represents only 3.3% of all patients with myeloma[2]. Only a few cases have so far been described[1-4]. Our experience with two cases of anaplastic myeloma may therefore be instructive.

Case Reports

Patient 1: A 46 year old man presented with history of back pain of 3 months duration. On clincial examination, he was very sick and pale with bilateral pedal oedema. He had tenderness over the right lower ribs and thoraco lumbar spine. Rest of the physical examination was normal. The haemoglobin was 5.6 gm%, total leucocyte count was 5700/mm^3 with a normal differential count and platelet count was 56,000/mm^3. Erythrocyte sedimentation rate was >160mm/hour. The serum chemistry was as follows: Blood urea: 160 mg/dl, serum creatinine: 11mg/dl, total protein: 6.6mg%, albumin:3.5%, globulin:3.1gm%. The liver enzymes were normal. Urine was positive for Bence Jone's protein. Radiograph of the chest showed expansile lytic lesions on the 4th ,8th and 9th ribs on the right side. Spinal x-ray showed collapse of L1 vertebra. Serum immunoglobulin (Ig) G was 6.9g/L, Ig A 0.67g/L and Ig M 0.23g/L. Bone marrow study showed hypercellular marrow with highly atypical plasma cells with marked pleomorphism, polylobate forms, multinucleation and plenty of plasma blasts. Normal elements were markedly reduced. This picture was morphologically consistent with anaplastic multiple myeloma (Figure I). He was started on supportive treatment for the renal failure and anaemia. However, before we could start chemotherapy, he died on the 4th admission day.

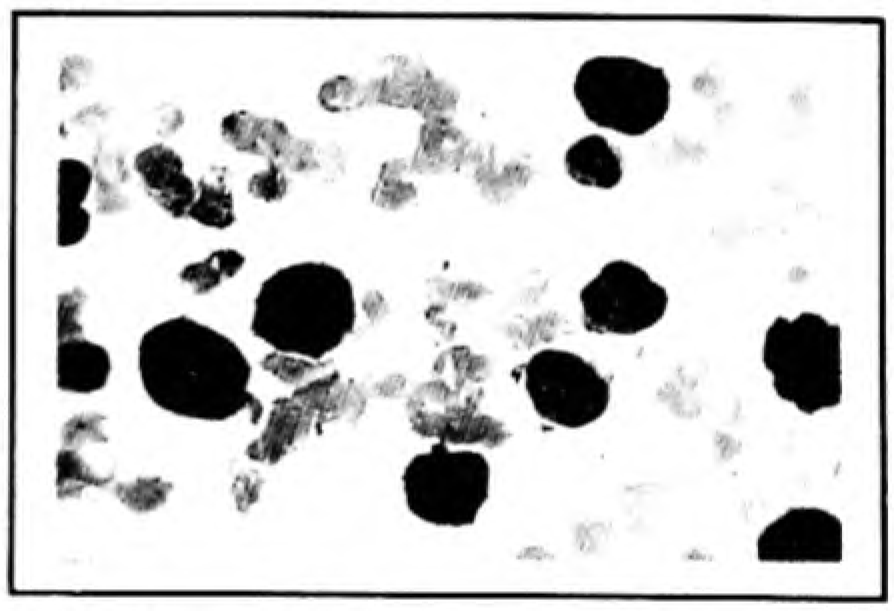


Fig 1 Bone Marrow aspirate smear showing large atypical plasma cells with bi and tribbed nuclei (Leish man x 1000)

Patient 2: A 60 old man presented with a history of a growth overlying year the right upper alveolar region since one moth. On clinical examination his general condition was satisfactory. There was a proliferative growth involving the right upper alveolus and adjacent hard palate extending from the region of the right upper canine to the last molar tooth. Lymph nodes were not palpable. Rest of the systemic examination was normal. Computed tomography (CT scan) of the face showed a soft tissue mass in the right maxilla with destruction of floor and anterior wall of the right orbit. Nasal cavity was involved on the right with destruction of middle and inferior turbinates. A biopsy taken from this lesion revealed plasmacytoma. A subsequent serum immunoelectrophoresis, bone marrow study and skeletal

From the Department of Medical Oncology (Geetha) **Pathology** (Nileena) **and Radiation Oncology (Sarah, Koilparampil, Prof. Rajan) Regional Cancer Centre, Thiruvananthapuram, Kerala, India.**

Received November 1998 Accepted March 1999

Correspondece to : Dr. Geetha N, MD,DM. Asstt. Prof. of Medical Oncology Regional Cancer Center Thiruvananthapuram-695011 Kerala, India Email- rcctvm@nda.vsnl.net in.

survey were normal. A diagnosis of solitary plasmacytoma was made and he received field radiotherapy to the right maxilla to a dose of 5500 cGy in 25 fractions over five weeks. Three months later he presented with a pathological fracture of the right humerus and was evaluated for disseminated disease. Skeletal survey showed osteolytic areas in the skull and left femur. Serum electrophoresis showed normal protein pattern. A bone marrow trephine biopsy study revealed hyper cellular marrow replaced by highly atypical plasma cells with prominent nucleoli and multi nucleated cells arranged singly and in sheets. Normal elements were markedly reduced. This picture was morphologically consistent with anaplastic myeloma. He was started on chemotherapy with vincristine, melphalan, cyclophosphamide and prednisolone. There was only minimal response and he died after three months.

Discussion:

Anaplastic myeloma is an uncommon variant of multiple myeloma which differs clinically and morphologically from classical multiple myeloma[3,1]. Clinically anaplastic myeloma is characterised by rapid, progressive disease and large extramedullary tumor masses developing in different organs[4,5,6]. Anaplastic myeloma may occur 'denovo' as in patient 1 or more often develops when multiple myeloma is in remission[3,4,6]. In a review of anaplastic myeloma Allen et al found that the median age at initial diagnosis of multiple myeloma was 53 years, suggesting that the aggressive phase develops in younger patients[7]. Quite a number of patients had Ig A gammopathy[7].

Suchman et al had described 7 patients with multiple myeloma who experienced an aggresive terminal phase characterised by rapidly enlarging soft tissue masses and tumor morphology characterissed by anaplasia[5]. Bournates described a 44 year old man with anaplastic myeloma who developed soft tissue masses as part of progression. Two patients in remission developing prominent extramedullary disease with anaplastic cells were described by Foucar[4]. DNA flow cytometric studies revealed the tumor cell population to have high degree of hyperdiploidy and high proliferative activity[4]. A case of 'denovo' anaplastic myeloma has also been described[8].

Plasma cell myeloma has long been recognised to transform to a morphologically more anaplastic and clinically more aggressive form of the disease[2]. It is hypothesized that the aggressive phase represents part of the natural history of multiple myeloma analogous to the terminal transformation associated with other relatively indolent myeloproliferative and lymphoproliferative disorders[7]. The diagnosis of anaplastic myeloma is usually established on the basis of morphological findings and progressive clinical picture. Anaplastic myeloma is characterised by the presence of blast cells in bone marrow or in other organs in clustered or diffuse forms. It is sometimes diffcult to distinguish anaplastic myeloma from high grade malignant lymphoma. Electron microscopic and immunohistochemical studies help in such situations[2,3,6].

Anaplastic myeloma has a bad prognosis. Radiotherapy in combination with aggressive chemotherapy is usually unsuccessful in patients with anaplastic myeloma[3,4,5]. Median survival of patients developing anaplastic myeloma is only 4 months[5]. In the present report also both patients were dead within 6 months. In view of the extreme poor prognosis and lack of response to conventional chemotherapy, patients with anaplastic myeloma should be considered candidates for innovative treatment.

References:

1. Kyle RA. Multiple myeloma. Review of 869 cases. Mayo Clin Proc. 1975;50:29-40.
2. Strand WR, Banks PM, Kyle RA. Anaplastic plasma cell myeloma and immunoblastic lymphoma. Clinical, pathologic and immunologic comparison. Am. J. Med. 1984:76:861-867
3. DiStasi M, Cavann L, Paties C et al. Anaplastic myeoloma. Extramedullary relapse of Multiple Myeloma in remission. Case report and review of literature. Acta Haematol 1986;76:202-207.
4. Foucar K, Raber M, Foucar E, Barlogie B, Sandler CM, Alexanian R. Anaplastic myeloma with massive extramedullary involvement; report of two cases. Cancer 1983;51:166-174.
5. Suchman AL, Coleman M, Mouradian JA, Wolf DJ, Saletan S. Aggressive plasma cell myeloma. A terminal phase. Arch. Intern. Med 1981;141:1314-1320.
6. Bourantas K, tsiara S, Christon L, Mitsi-Malamou V. A case of Anaplastic myeloma. J Expt. Clin. Cancer Res. 1994;13:269-273.
7. Allen G SL, Coleman M. Aggressive phase multiple myeloma. A terminal analplastic transformation resembling high grade lymphoma. Cancer - Invest 1990; 8:417-424.
8. Zervas K, Constantinon N, Karakantza M, Tsigalidon - Balla V. Asnaplastic myeloma. Leuk-Lymphoma 1995;16:515-518.

OMENTAL LIPOBLASTOMA: A CASE REPORT

Nasib C. Digray, M.S., M.Ch.; Yogeshwar Mengi, M.S., M.Ch.; Thappa D.R., M.S.; Goswamy H.L. M.S., M.Ch.

***Abstract:** A rare case of intra-abdominal lipoblastoma arising from omental fat, in a 14 months old male child is presented. Since part of the tumour was densely adherent with splenic vessels, complete excision necessitated concomitant splenectomy. Two years after surgery, the child is free of any tumour recurrence and post-splenectomy complications.*

***Key words:** Lipoblastoma, Omentum, Splenectomy.*

JK-Practitoner 1999; 6(3): 236-238

Introduction:

Lipoblastoma is a rare variety of soft tissue tumour affecting children below 3 years of age[1-6]. Abdominal presentation of this tumour is occasionally reported, whereas the majority are reported in the trunk area[2-6]. A review of literature till 1996, revealed that only 7 out of 87 tumours were arising from intra-peritoneal fat[6].

Case Report:

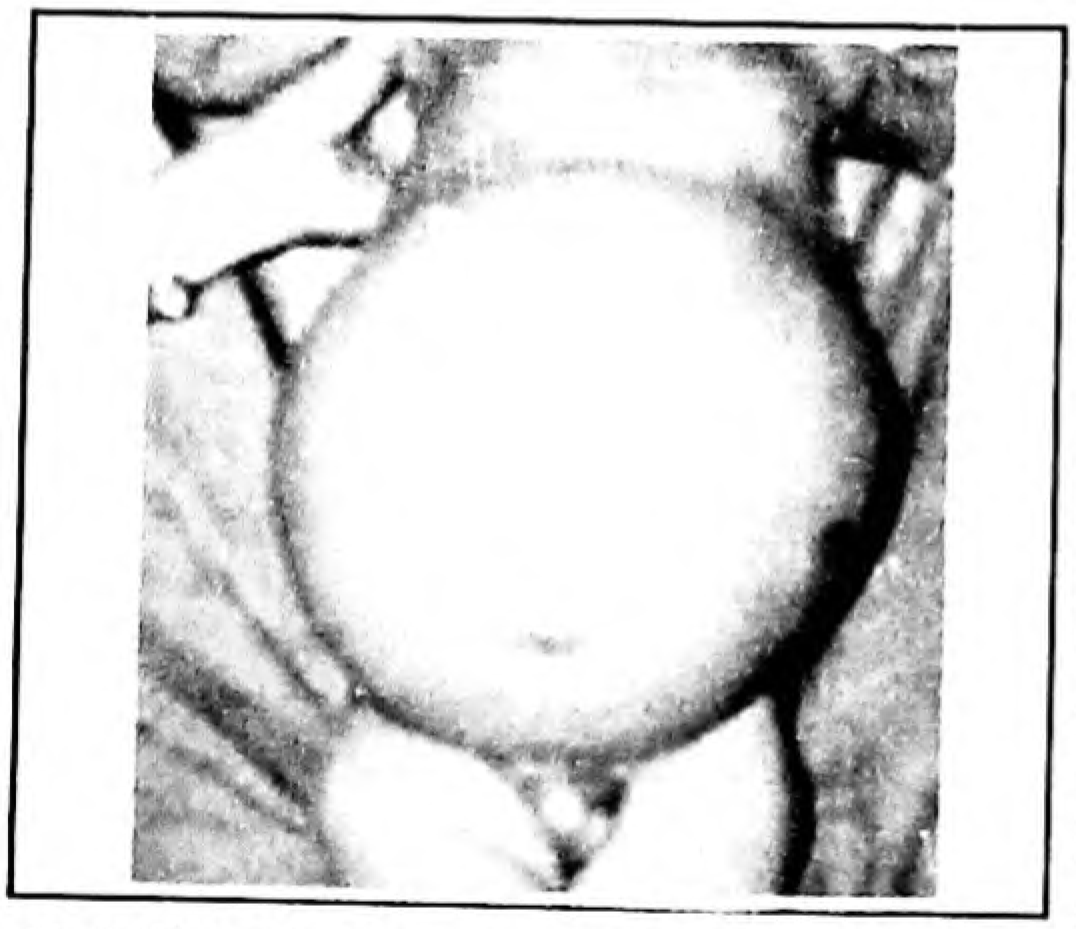


Fig.1: Clinical Photograph of a patient showing massive abdominal swelling due to omented lipolilastoma

A 14 months old male child presented with progressive abdominal enlargement of 6 months duration. The baby otherwise was thriving well and did not have any obstructive bowel symptoms. Examination revealed a healthy child with non-tender symmetrical distention involving almost whole of the abdomen (Fig.I). Routine laboratory workup was normal. X-ray of the abdomen revealed a soft tissue mass pushing gut coils downward into the pelvis. Ultrasound showed a large solid mass (15x12x10 Cms.) of high echogenic nature, arising from the omentum. The mass was well defined except at the splenic hilum. Fine needle aspiration cytology (FNAC) revealed fatty cells comprising of mature adipocytes and lipoblasts. CT scan of the abdomen could not be done. At laparotomy, a large lobulated tumour arising from the greater omentum was found. The tumour was well encapsulated except at the splenic hilum where it was densely adherent to the splenic vessels. No definite vascular pedicle supplying the tumour could be isolated. Complete excision of the tumour was done with concomitant splenectomy (Fig.2). Rest of the abdominal viscera and lymph nodes were normal. Post-operative period was uneventful. The biopsy of the resected tumour showed a picture of benign lipoblastoma. The patient was immunized with anti-pneumococcal vaccine and put on chemoprophylaxis with long acting penicillin. He is free of any tumour recurrence and post-splenectomy complications after 2 years of follow up.

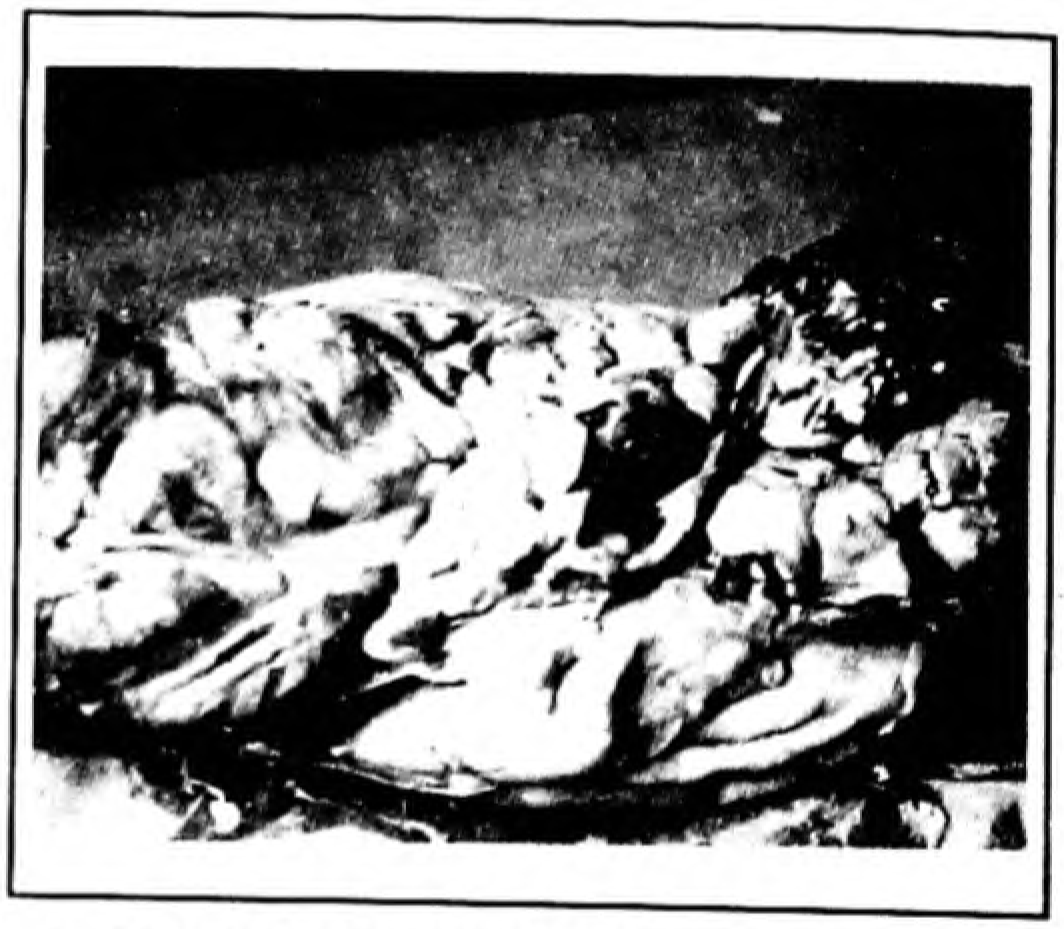


Fig.2: Excised specimen of lipoblastoma neighing 1.2. kg. Note the extension of the tumour to the splenic hilum (Arrow).

From the Department of Division of Pediatric Surgery, Department of Surgery, GMC, Jammu, J&K. India (Digray, Mengi, Thappa, Goswamy)

Received November 1998 Accepted March 1999

Correspondence to : Dr. Nasib C. Digray, 220-Sarwal Colony, Jammu, J&K. India 180 005.

Discussion:

Lipoblastoma and lipoblastomatosis are benign tumours of adipose tissue occuring in children below 3 years of age[1-6]. Whereas a lipoblastoma is a well encapsulated and circumscribed and easily resectable lesion, lipoblastomatosis represents a more diffuse, infiltrating tumour with a tendency for local recurrence even after attempted complete resection[1,2,4]. On histological examination, both lipoblastoma and lipoblastomatosis are identical with lobular arrangement of fat cells that vary from mature lipocytes to lipoblasts and perilipoblasts, sometimes mimicking a lipoma or well differentiated liposarcoma[1,3], requiring DNA cytometry to rule out malignancy[6]. Abdominal lipoblastomas, which are very rare, present as progressively or rapidly growing abdominal swellings. Although an ultrasound examination may pick up the diagnosis of these lesions, CT scan and MRI are more specific in defining their extent and feasibility of complete excision[5,6]. Surgical treatment of lipoblastoma is complete excision. However in some cases, the tumour may be adherent to the major vessels/vital structures requiring a careful dissection[6]. In our patient where part of lipoblastoma was adherent to the splenic vessels, splenectomy could not be avoided inspite of our best efforts. However this should be taken as an exception rather than as a rule in majority of patients with lipoblastoma.

References:

1. Arda IS, Senocak ME, Gogus S et al. A case of benign intrascrotal lipoblastoma clinically mimicking testicular torsion and review of literature. J. Pediatr. Surg. 1993;28:259-261.
2. Beebe MM, Smith MD. Omental lipoblastoma. J.Pediatr. Surg. 1993; 1626-27.
3. Chung EB, Enzinger FM. Benign lipoblastomas: an analysis of 35 cases. Cancer. 1973;32:482-492.
4. Dharan M, Siplovich L. Intra-operative cytology of lipoblastoma. A case report. Acta Cytol. 1993;37:563-565.
5. Norton KI, Glajchen N, Dolgin SE. Magnetic resonance appearance in a case of lipoblastomatosis. Pediatr. Surg. Int. 1996;11:286-287.
6. Trobbs RB, Meier T, Nenning H et al. Benign mesenteric lipoblastoma. Pediatr. Surg. Int. 1996;11:425-426.

CHECKLIST FOR SUBMISSION OF MANUSCRIPT

- Covering letter including copy-right release
- Three copies of manuscript on A-4 size paper
- Name and address of author responsible for correspondence about the manuscript, including highest degree and affiliations of each author.
- Abstract (upto 150 words) along with 3-6 key words
- Running title (5-6 words)
- Three glossy prints for each illustration (10 cm × 8 cm), appropriately labelled and each illustration is cited in the text. Submit the legends on a separate sheet in the manuscript.
- Check all references for accuracy and completeness. Put references in proper format in numerical order, making sure each is cited in the text.

ANGIOMA SERPIGINOSUM

Qazi Masood M.D.; Sheikh Manzoor M.D.; Iffat Hassan M.D.

***Abstract:** Angioma serpiginosum is a rare naevoid disorder primarily affecting the small vessels of the upper dermis. Here we report a case of angioma serpiginosum in a nineteen year old female in view of the rarity of this condition.*

***Key words:** Angioma Serpiginosum, Naevus.*

JK-Practitioner 1999; 6(3): 238

Introduction:

Angioma serpiginosum is a rare naevoid disorder, characterized by progressive, noninflammatory ectasia of superficial dermal capillaries and has been infrequently reported in the literature[1].

Case Report:

A nineteen year old female, product of a non-consanguinous marriage, presented with erythematous lesions all over the body since birth. There was no history of itching or bleeding from the lesions. Family history was noncontributory. Her systemic examination was unremarkable. Cutaneous examination revealed dull red patches, variable in size and configuration, composed of tiny capillary puncta with numerous outlying, discrete and grouped capillary tufts no larger than a pinhead. (Fig.I). Lesions were mainly concentrated over buttocks and legs. Diascopic pressure produced only partial blanching. Examination of hair, nails, teeth and mucous membranes was unremarkable. Her routine investigations including hemogram and coagulogram were within normal limits. Skin biopsy from one of the representative lesions revealed a normal epidermis with thin walled telangiectatic blood vessels within the dermal papillae. Rest of the histopathollogical examination was noncontributory.

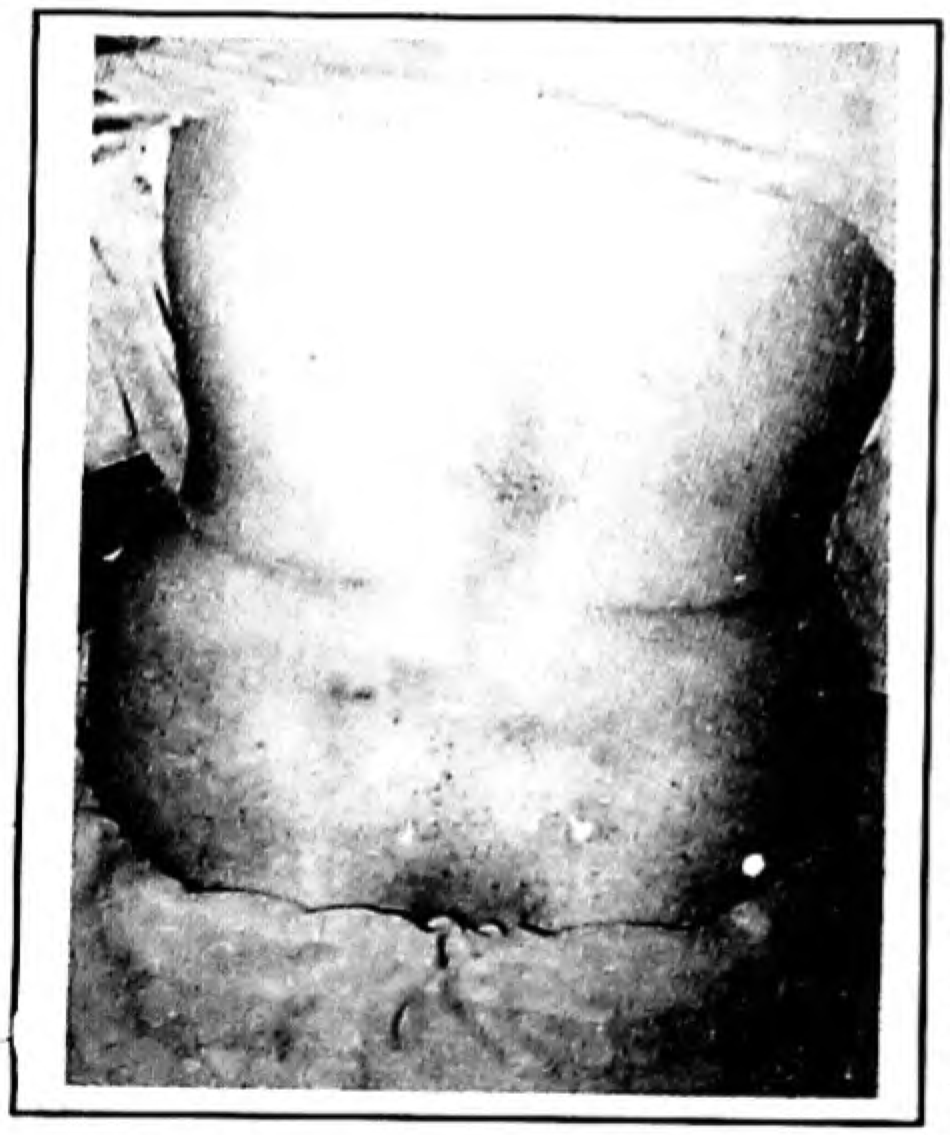


Fig. 1: Angioma Serpiginosum

Discussion:

Angioma serpiginosum, a rare naevoid disorder was first described by Hutchinson in 1889 and named by Crocker in 1894[2]. The disease usually starts in childhood and has a predilection for female sex. Most of the cases are sporadic but an autosomal dominant inheritance has also been reported[3].

The disease starts as pinhead sized capillary puncta which progress by development of satellite punctate lesions. Frequently there is a background of more diffuse erythema which is due to dilatation of the subpapilllary venous plexus. Individual puncta often disappear spontaneously and complete regression may occur or traces may persist indefinitely[1].

Although all parts of the body with the exception of mucous membranes have been reported to be affected yet, the condition has a predilection for the lower limbs as was also evident in our patient. Being a product of a nonconsanguinous marriage with a negative family history, our patient seems to have acquired the disorder in a sporadic fashion.

References:

1. Yaffee HS. Angioma Serpiginosum, Arch Dermatol 1967;95: 667.
2. Crocker HR: Lymphodermia Perniciosa. Br J Dermatol 1894;6:367.
3. Marriot PJ, Munro DD, Ryan T: Angioma Serpiginosum-familial incidence Br J Dermatol 1975;93:701-6.

From the Department of Dermatology, STD & Leprosy Government Medical College Srinagar-Kashmir (Masood, Manzoor, Hassan)

Received November 1998 Accepted March 1999

Correspondence to : Dr. Qazi Masood, Associate Professor and Head, Department of Dermatology, STD & Leprosy Govt. Medical College Srinagar.

AORTO-CAVAL FISTULA: A CASE REPORT

M.Akbar Bhat, M.Ch.; K.S.Neelakandhan M.Ch.; Unnikrishnan Menon M.Ch.; Vijit Koshy Cherian M.S.

Abstract: *Despite the well characterized physiological effects of aortocaval fistulas, patients with such uncommon lesions may manifest a diverse array of symptoms and diagnosis is often delayed or overlooked. Emergent surgical intervention was performed in a case of atherosclerotic infrarenal abdominal aortic aneurysm with aortocaval fistula. Aortocaval fistula was closed with interrupted pledgetted sutures and the aortic aneurysm was repaired with bifurcation dacron graft. Patient's deranged cardiac and renal function returned to normal in the early postoperative period.*

Key words: *Aortocaval fistula, Abdominal aortic aneurysm.*

JK-Practitioner 1999; 6(3): 239-240

Introduction:

An arteriovenous fistula involving the abdominal aorta and adjacent inferior vena cava is a rare sequela of spontaneous aneurysm rupture into adjacent venous system or retroperitoneal injury to these major vessels.

Spontaneous rupture of abdominal aortic aneurysm (AAA) into the adjacent vena cava occurs in less than 1% of all aneurysms and about 3% of ruptured aortic aneurysms[1]. Factors influencing the clinical manifestations include the origin, size, location and duration of the fistula. Since this complication (Aorto-caval fistula) may present atypically leading to delay in diagnosis and management[2]. The key to the diagnosis is suspicion of the complication in every case of aortic aneurysm likely to have ruptured. We present a case of aorto caval fistula in a patient having abdominal aortic aneurysm.

Case Report

A 52 year diabetic male patient presented with dysuria and bilateral pedal edema over a period of 2 weeks. Patient had periumblical expansile pulsatile mass with a thrill. Patient was normotensive withnormal lower limb blood pressure. The renal parameters were deranged (BUN 42mg%, serum creatinine 1.72mg% and ceratinine clearance 28.9ml/min). CT scan showed a leaking AAA with iliac vein thrombosis. Ultrasonography showed AAA with IVC occlusion and right psoas collection. However the clinical suspicion of leaking AAA with aortocaval fistula was confirmed on aortography.

Emergent exploration was undertaken and infrarenal AAA just above the bifurcation of aorta found. The aneurysm had a communication of 6 x 4mm on the posterolateral aspect with the inferior vena cava. The inferior vena cava was pulsating like an artery. There was no thrombus in inferior vena cava.

After achieving control proximal to the AAA, both common iliac arteries were clamped. Distal IVC was controlled with sponge-stick and common iliac veins with finger pressure. The aneurysm was opened directly and clots/debris evacuated. The fistulous tract was closed with interrupted pledgetted sutures (3/0 prolene with teflon pledgetts). Aorto-iliac bifurcation graft 16/8mm Dacron was anastomosed to aorta proximally and common iliac arteries distally.

Postoperative recovery was uncomplicated and patient had normal cardiac and renal parameters. Postoperative aortogram showed satisficatory results. The patient has a two year followup, without any sign of cardiac or renal failure as well as arteriovenous insufficiency of legs.

Discussion

Aortocaval fistula is a rare complication of rupture of aortic aneurysm into inferior vena cava. The incidence of aorto caval fistula is <1% in aortic aneurysms[1]. Most of such aneurysms are arteiosclerotic. Other reported causes of aortocaval fistula are rupture of syphilitic/mycotic aneurysms, marfans syndrome, Ehler-Danlos syndrome or Takayasu arteritis and penetrating injury due to stab or gun shot wounds[1]. The diagnosis of aortocaval fistula is performed by typical clinical features. Pathognomonic is the hisoty of pain, large pulsatile abdominal mass, machinery like abdominal

From the Department of Cardiovascular and thoracic surgery Sree Chitra Tirunal Institute of Medical Sciences and Technology, Thiruvanathapuram, Kerala, India (Bhat, Neelakandhan, Menon, Cherian)

Received February 1999 Accepted March 1999

Correspondece to : Dr. M.Akbar Bhat, Consultant CVTS, SKIMS, P.B.No.1061, GPO Srinagar 190001, Kashmir (India).

bruit and acute dysponea. Pedal edema and renal insufficincy occurs due to markedly elevated venous pressure[2,3]. Prompt surgical repair is mandatory. Any measures to improve cardiac and renal function are of no avail. Reported operative mortality has been 21-55% in the review by Alexander and Imbembo[4]. Most of the deaths are due to delayed/improper diagnosis leading to excessive bleeding, prolonged hypotension and complicated postoperative period[5,6,7].

Aortography is the gold standard for the diagnosis of aortocaval fistula. Ultrasonography and CT scan may miss the diagnosis[8]. Proper clinical acumen, complied with timely surgical interrvention should salvage all the cases of aortocaval fistulae.

References:

1. Brewster DC, Cambria RP, Moncure AC, et al. Aorto caval and iliac arteriovenous fistulas. J Vasc. Surg 1991; 13:253-65.
2. Petitin L, Pelouze A, Mercier V, et al. Rupture of abdominal aortic aneurysm into inferior vena cava. Ann. Vasc. Surg. 1987;1:572-7.
3. Johnson JM, Wood M. Arteriovenous fistula secondary to rupture of atherosclerotic abdominal aortic aneurysm: report of five cases. Am. J.Surg 1978;136:171-5.
4. Alesander JJ, Imbembo AL. Aorto-vena cava fistula. Surgery 1989;105:1-12.
5. DeBakey ME, Cooley DA, Morris GC Jr, Collins H. Arteriovenous fistula involving the abdominal aorta. Ann Surg 1958;147:646-58.
6. Lehman P. Spontaneous arteriovenous fistula between the abdominal aorta and inferior vena cava. Ann Surg 1938;108:694-700.
7. Weinbnaum FI, Riles TS, Imparato AM. Asymptomatic vena cava fistulization complicating abdominal aortic aneurysm. Arch Surg 1975;110:806-12.
8. Davidovi CL, Petrovi CP, Lotina S, et al. Aorto caval fistula due to abdominal aortic aneurysm rupture. Srp Arch Celok Lek 1997 Nov-Dec; 125(11-122): 370-4.

JK-Practitioner

Get a

Free Copy

for your library

Make sure new ideas and information flow freely to your colleagues and students.

Complete and return the Library Recommenoation Form printed below, and we will send you a complimentary copy of **JK-Practitioner** for your institutional library.

To: Collections Development Librarian

Name of Library ____________________
Name of institution ____________________
Street address ____________________
City, State, Code ____________________

From:

Your name ____________________
Street address ____________________
City, State, Code ____________________

APPENDICITIS SECONDARY TO FOREIGN BODY IMPACTION

Iqbal Saleem Mir M.S.; Javed Naqshi M.S.; Anjum Malik M.B.B.S.; Shoukat Jeelani M.S.;
Ghulam Hassan M.S.; Ashiq Hussain Naqashbandi M.Ch.

Abstract: Even though appendicitis is the common surgical disorder met in the emergency, appendicitis secondary to an ingested foreign body is quite rare. The most common foreign body being the common pin. We present the case of a 40 years old male who developed an appendicular lump secondary to accidental ingestion of a common pin. The patient was managed on conservative lines and later operated after an interval of 6 weeks. The patient had a smooth post-operative period.

Key words: Appendicitis, Foreign body, Lump.

JK-Practitioner 1999; 6(3): 241-242

Introduction:

Acute appendicitis is the most common surgical emergency encountered by surgeons all over the world. One of the rare causes of appendicitis is due to ingested foreign bodies getting impacted in appendix. The most common foreign body being a common pin, and usual patients being children[1].

We herein present our experience of such a case in an adult who had accidently ingested a common pin 3 months prior to developing mass in Right Iliac fossa. During investigations, it was found that the pin had lodged in the appendix to cause an appendicular lump. The patient was managed conservatively. He was operated 6 weeks later and all appendix along with the pin was removed. The post operative period was uneventful.

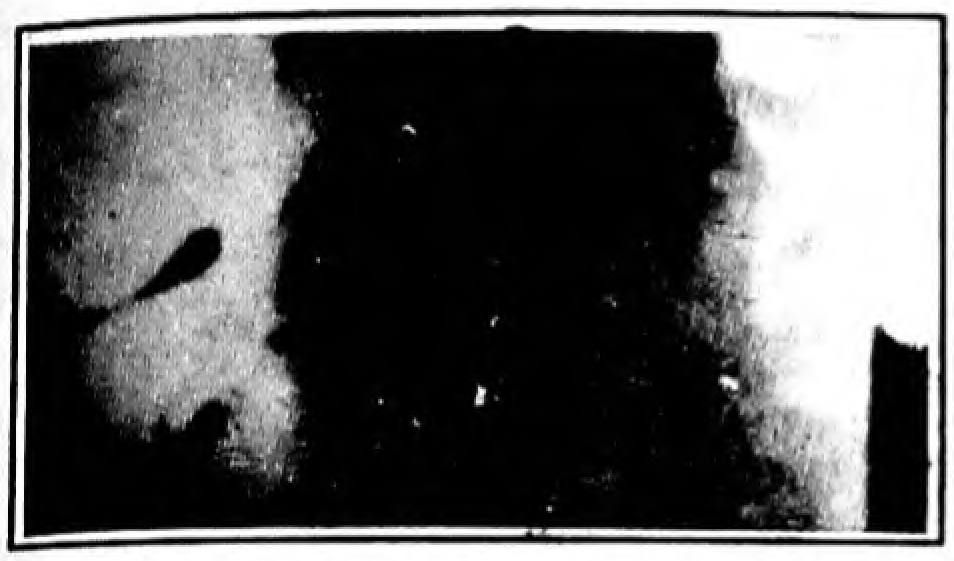


Fig I. Barium study showing common pin outside ceacal wall

A similar case was reported by Jatal in 1995 in India[1].

Case Report

A 42 years old male was admitted in Surgery Department of SMHS Hospital, in Feb. 98 with compliant of pain R.I.F. for 3 days and vomiting once. The patient had been taking some antispasmodics for what he termed as 'Abdominal colic'. The past history of the patient revealed that he had ingested a common pin approximately 3 months back while working. He was not sure about the evacuation of the ingested pin.

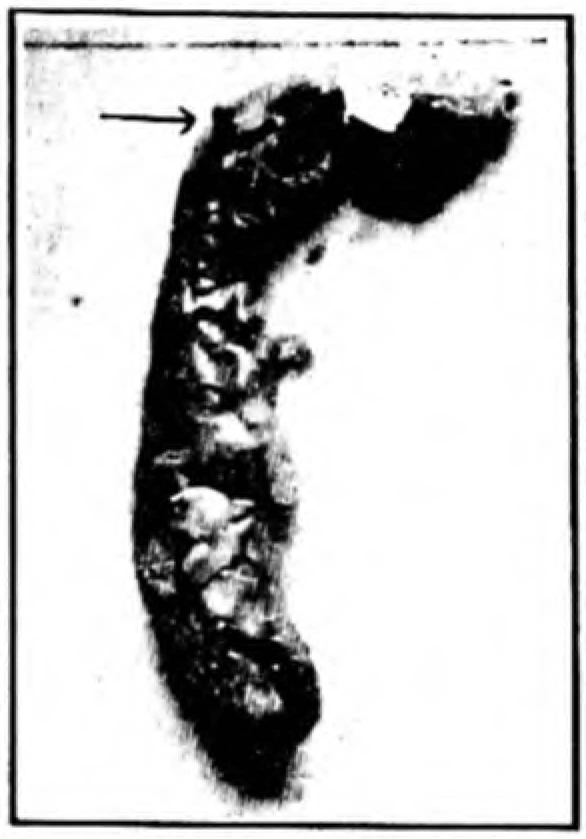


Fig 2: Appendix with Pin (arrow).

On examination the patient was of strong build. The pulse was 80 beats/min. Examination of Abdomen revealed a tender and firm lump in the Right Iliac fossa which was fixed.

The investigations revealed a Hb value of 11 gm% with T.L.C (12,500) and D.L.C ($P_{80}L_{19},E_1$). The urine of the patient was normal.

An X-ray of lower abdomen revealed a shadow of a common pin with calcification around it in the R.I.F. An USG of Abdomen confirmed the presence of Appendicular Lump 4.1x3.0 cms with some hypoecoic shadows in it (?fecoliths).

A preliminary diagnosis of 'resolving appendicular lump' was made. The patient was treated on conservative lines as advocated by Oshner and Sherren. The patient responded to treatment and was discharged.

In the follow-up the patinet underwent a Barium follow through study (Fig-I). This confirmed the presence of pin in the appendix outside the ceacal wall. The patient was dated for Interval appendicectomy after 6 weeks.

On readmission the abdomen was explored via a lower paramedian incision. It was found that the pin was

From the Department of Surgery, GMC, Srinagar Kashmir (India) (Mir, Naqshi, Malik, Jeelani, Hassan, Prof. Naqashbandi)

Received Arpil 1999 Accepted June 1999

Correspondece to : Dr. Iqbal Saleem Mir, C/o Taj Studios, Lal Chowk, Srinagar, Kashmir.

lodged in the appendix. The point of the pin was near the tip of appendis (Fig 2). Appendicectomy was performed. The patient had a smooth post operative period and was discharged after 4 days. In the follow-up of 6 months remained in excellent health.

Discussion:

Even though appendicitis is the most common cause of "Acute Surgical Abdomen". Appendicitis Secondary to foreign bodies constitute only 4% of all cases[1,2,3]. Balch and Donald reported that 225 cases of foreign bodies in the appendix as folowing 81 pins, 47 lead shots, 34 seeds, 16 bone pieces and 47 miscellaneous objects[4]. Usually the foreign body is ingested by children but in our case the patient was a 42 years old male who had accidentally swallowed the pin while at work.

The ingested foreign body gravitates to the most dependent part of the ceacum and can enter the lumen of appendix. In cases of common pins the rounded tip usually enters first due to its relative heaviness, but in our case the tip has entered first causing appendicitis with formation of a lump.

An x-ray abdomen picked up the foreign body image even though other authors report that this is rare[5].

In our case we had to manage that patient on conservative lines followed by interval appendicectomy.

The patient remained well in the post operative period.

The authors are of the view that Appendicectomy is the treatment of choice in cases of appendicitis secondary to foreign bodies.

Acknowledgment

The authors wish to thank Mr. Manan and Mr. Kulbir of Photographic section of Govt. Medical College, Srinagar and Mr. Abdul Hameed and Mr. Ishrat of Excellent Computers, Batamaloo, Sriangar.

References:-

1. Jatal S.N: An unusual case of perforated appendicitis. Medifacts; 1995; 15:28.
2. Condon R.E.: 'Appendicitis' in the Textbook of surgery. Sabiston D.C.(ed) 13th edition W.B. Saunders company. Philadelphia. P. 968. 1986.
3. Ellis H. 'Appendix' in Maingot's Abdominal operation, Schwartz S.I, Ellis H. (ed's) 8th edition. Appleton-century-crofts, Connecticut, P.1258. 1985.
4. Balch. C, Donald S. Foreign bodies in appendix as reported by Jatal S.N. An unusual case of perforated appendicitis. Medifacts: 1995; 15:28.
5. Brooks DW, Killin D. A. Roentgenographic findings in acute appendicitis. Surgery 1965;57:377.

BOOK REVIEW

Heart Attack, Hypertension, Heart Trouble:- Booklets Published by Heart Care Association of Jammu and Kashmir Editor Dr. Nissar Ahmad Trali 1998.

It gives me immense pleasure to say that I gone through 3 booklets titled "***HEART ATTACK***", "***HYPERTENSION***" and "***HEART TROUBLE***". These booklets are edited by Dr. Nissar Ahmad Trali and published by `Heart Care Association of Jammu and Kashmir: These books are written in Urdu so that common man would also benefit. I find these books extremely useful, highly scientific, applied practical and of great use of young doctors, Clinicians and common people. These books are well intended as stress is laid on preventive aspects of Heart disease and Hypertension. I congratulate Dr. Nisar Ahmad Trali for his great effort and excellent work in the field of understanding prevention of Heart disease and Hypertension. I pray that he would continue his effort and produce more booklets on other common diseases of our State.

(Prof. Mohammad Yousuf) M.D.
Physician Specialist

A CASE REPORT OF VESICO-CUTANEOUS FISTULA

Imtiaz Shah M.S.; Metha K.S. M.S.; Sunil Raina M.B.B.S.

Abstract: Urinary cutaneous fistalae in the suprapubic area are extremely rare. We report two such cases.

Key words: Testicular tumor, bladder diverticulum, stricture.

JK-Practitioner 1999; 6(3): 243

History:

55 year male married, who had been labelled as a case of (R) testicular tumor and had undergone (R) sided orchidectomy 3 months before. In the follow up period, he started developing signs and symptoms of obstructive uropathy (straining on micturition with frequency) and within couple of days of these symptoms, patient developed a small fistula at the proximal end of the incision site in the (R) side of the hypogastrium (orchidectomy scar). The patient was put on antibiotics and anti-inflammatery drugs and suddenly patient comes with leaking of few drops of pus from the pustule site for which antiseptic dressing was done for few days but inspite of that the wound did not heal and drops of urine started leaking from the site.

Examination: There was a small opening in the distal end of the orchidectomy scar just lateral to the public tubercle.

Retrograde urethrogram reveals stricture in the proximal urethra.

U/S abdomen reveals huge capacity U. bladder with small diverticulam on (R) side with prostate about 24 grams and residual urine more than 170 ml.

Suprapubic cystogram revealed a small diverticulum with wide mouth on (R) lat. wall of bladder.

Internal urethrotomy with excision of the fistulous tract with indwelling catherization in situ for 2 wks. kept the patient free from obstructive urinary symptoms and dribbling of the urine from the site.

Comments:-

Urinary cutaneous fistulae in the suprapublic area is extremely rare and 2 cases of such fistulae at the thigh following pelvic trauma and one case following Retropublic prostatectomy-Prostatocutaneous fistula have been reported.

The series of events leading to the fistula formation at the suprapublic area are:-

i) (R) orchidectomy possibly infection inthe subcutaneous area.
ii) Strcture in the urethra.
iii) Significant residual urine in bladder adherence of diverticulum to the site of incision.
iv) Infection and fistula.

References:-

1. Moskovitz 'B' etal, Urethro-thigh fistule report of 2 cases Eur, Urol 1986;12:141-142.
2. Snooks S.J., Dharmasena F, Mitchell T.J., Crisp J.C. Prostatocutaneous urinary fistula to thigh after retropublic prostatectomy in patients with polycythemia rubra vera. Br. J. urol. 1986;58:558.
3. Sharma R.N; Shah I. Urethro inguinal fistule Ind. Juor of Urology 1989; 6 (1):.

From ASC Hospital (Shah, Metha, Raina) **Sidhra, Jammu (India)**
Received January 1999 Accepted April 1999
Correspondece to : Dr. I.Shah. Deptt. of Urology, Ascoms & Hospital Sidhra, Jammu.

TODAY THE SHEEP, TOMORROW THE SHEPHERED. IS THE CLOCK TICKING FOR A BIOLOGICAL HIROSHIMA?

M.A.Kamili M.D.; Nissar Ahmad Bhat M.D.; G.M.Malik M.D., F.A.C.G.; A.Nafae M.D.

Cloning is the production of an exact xerox copy of the organism. A photostat machine produces photographic copy of documents.Similarly cloning is a biotechnique for copying individuals by manipulations at cellular or microscopic level. Cloning means the production of exact genetic replicas of an individual. In case of cloning genes from a single parent are used to produce an identical copy. There are two types of cloning-Gene cloning at a molecular level and cloning of organisms. Gene cloning is done in three stages—the targeted gene in a cell is first isolated, then the isolated gene (biochemically a fragment of DNA) is introduced indifferent living organisms and lasty, it is ensured that the recipient accepts the donor gene and inherits its properties. Cloning of organisms is slightly of different kind. In the organism cloning the nucleus of haploid cell, ovum, is replaced by nucleus of diploid cell. This is then made to undergo normal process of growth within the mothers body. Thus mother delivers a clone of itself at the end of pregnancy. A clone is essentially a population of individuals, all of whom have descended from a single ancestor.Parentage is a single parentage and not dual parentage. You do not need mixing of two sexes in order to produce a clone. You mix genes. There is a genetic identity among the clonal population themselves and between them and the parent. This has been the way the populations have proceeded ever since the very first living organism started on the earth perhaps about 3.8 billion years ago. A clone is an identical copy of a single ancestor or identical young individual of a single parent and thus cloning is a form of a sexual reproduction common in lower organisms like certain plants.

Cloning generally involves transplantation of a nucleus from body cells or embryonic cells into an enucleated unfertilized egg in the lab, thereby bypassing the usual process of fertilization of egg by sperm. In the usual process of reproduction the sperm nucleus fuses with the egg nucleus resulting in doubling of the chromosome number in egg (zygote). This doubling is believed to trigger mitosis (cleavage) in zygote. In cloning nucleus of egg is replaced with a nucleus of body cell which contains the full component of chromosomes to trick the host egg cytoplasm to initiate mitosis. In general animals and humans do not even go through the clonal mode of propagation.

Earlier investigations on sea urchins, amphibians and man had shown that the individual cells possess the capacity to develop into a normal offspring-a phenomenon called totipotency. Hans Driesch was the first investigator to demonstrate in 1891, the totipotency of early embyronic cells at 2 cell or 4 cell stage.

Dr. Ian Wilmuts Experiment

In 1995, Dr. Ian Wilmut and his team of researchers at Roslin institute in Edinburgh (Scotland) took udder cells from a six (6) year old female sheep-a Fin Dorset Ewe and placed it in a special solution that controlled its division or cell cycle. The cell was deprived of certain nutrients. At the same time an unfertilized egg was obtained from another adult sheep. Its nucleus was carefully removed leaving the cytoplasm intact. The nucleus of udder cell was taken out and transfered into the enucleated egg. Subsequently the transplanted nucleus became functional according to new surroundings (egg cytoplasm) in which it had been artificially placed. This viable combination underwent cleavage like that of a normal zygote. The resulting embryo was then transplanted into the uterus of a third adult sheep (surrogate mother) for its further development.

The first sheep (clone mother) was a pregnant sheep so its udder cells were at an active stage of the reprodductive period of the sheep. The second sheep (egg mother) was an adult fertile female having egg cells equipped for fertilization and embryonic development. The third sheep (surrogate mother) was also a female of reproductive age group who was given harmonal treatment to prepare her for accepting the embryo in her uterus for further development. The process was not easy. Dr. Ian Wilmut had fused 277 udder cells with an equal number of eggs but that only 29 of the eggs had

JK-Practitioner 1999; 6(3): 244-246

From the Department Medicine SMHS Hospital and Govt. Medical College, Srinagar. (Kamili, Bhat, Malik, Nafae)

Received Feburary 1999 Accepted April 1999

Correspondence to : Dr. M.A. Kamili, 52-Balgarden, Srinagar Kashmir (J&K) India Pin - 190010.

developed into embryos. When he transfered these embryos to the sheep who were the prospective surrogate mothers, only 13 became pregnant. Of these 13, only one carried the pregnancy to term and subsequently a normal healthy little lamb-Dolly-was born in February 1996. The new born sheep was genetically similar to the "clone mother" from which nuclear DNA was taken for transplantation. However it does not have any genetic similarity with the sheep from which the egg was taken or the "surrogate mother" because they did not contribute any nuclear DNA in the process.

In an earlier experiment Wilmut and his associates had produced identical lambs by using embryonic cells of the sheep. But for Doly, they exploited the hidden totipotency of the entire set of genes of a fully differentiated cell. In 1996 Dr. Donald Wolfe and his team at Oregon Regional Primate Centre in USA successfully cloned a Rhesus monkey while Prof. Lu Guangxin of the Human Reproductive Engineering Laboratory, Human University Beijing, cloned laboratory rats.

Could we have Human Clones

We humans are rather interesting, being products in our existence, not only of our genes that we get from our parents but also of what we receive during the course of our life time from the external world. Most human behavioural traits are acquired or learned and only a few are instinctive (gene born). Human clones if produced in future would not be behaving identically with their donor parent. Human clones cannot be identical not even if they have the same Horoscope. Even if you were to clone humans,the two cloned humans will have two separate souls, so two homozygous identical twins will certainly have two different thought patterns depending on their experiences. Human cloning may lead to dangers of inbreeding, and frequency of homozygous individuals afflicted with disorders may increase following marriages between heterozygote clones. Thus cloning may adversely affect genetic diversity and consequently reduce body resistence to diseases as seen in monocultures. Human cloning would discard sexual participation of male partner in reproduction. Cloning of plants and animals, therefore, may be more beneficial to mankind than human cloning.

Adding to the confusion is the recent announcement of plans by a Chicago scientist to clone humans as a means to fight infertility. It also does not gaurantee that the cloned individual will be identical in all respects with the donor including behaviour and talents which are not genetically determined. On the other hand, if successful, it may lead to abnormal shifts in the sex ratio as it will offer an assured method to choose the sex of the child, with disastrous social consequences. Recent announcement by the US president and the E.C. countries to ban human cloning research is a step in the right direction. But it may not be enough, unless such research is banned by all countries, the threat of creating Frankenstein's monster will remain. Human cloning had led to worries, ranging from dictators to ultra intellectuals cloning themselves, to the possibility that societies might one day try to create "master races" of eugenically selected perfect human beings. Scientists are working all over the world and have set a target date of 2005 to identify every single gene in the human genetic code. Once this is achieved, it would be possible to think of altering genes and creating designer babies with predetermined characteristics. These can then be cloned. Scientists have to wait for improvements in technology to make cloning more effective.

Cloning Future

We humans have a very large amount of DNA in our body. It is estimated that if you measure bases in DNA strip; it will be round about 3 billion bases. And man has about a hundred thousand to three hundred thousand genes. Each gene makes a protein, a gene might make an RNA, many traits etc. cloning of a particular gene could be useful. In fact it started being done about 1975 or so when people knew how to take a cell, take all DNA in it, clip just one particular gene that they were interested in, take it elsewhere, incorporate it in some place and ask it to produce whatever that gene produces. That is refered to as transgenics or genetic engineering. That is also a clone.

It is now possible to take the gene, let us say, insulin or interferon, stitch it into plants genome, grow the plant. It is the plant now plus the new gene. The Boycee Thompson Institute in Cornell has already got an edible vaccine that is being tested. What is done is e.g; take cholera microbe-get that particular part of cholera microbe protein which expresses a gene-put that in a banana so that what the banana does then is make its own fruit. In that fruit it also puts in the vaccine, or the antigen for cholera, for the cholera bacillus. Now a child can start eating a banana and along with banana it also ends up getting a vaccination for cholera. It is possible now, in the laboratory, to take skin cells and multiply them to produce a piece of skin almost as big as a post card.

Attempts are now being made to generate organs and specific tissue types from stem cells or germ cells. Professor John Gearhardt of the Johns Hopkins University at Baltimore, and his post doctoral associate, Michael Shamblott, have started with what are called embryonic germ cells (EG cells) from an aborted human foetus and attempted to direct these to produce one particular cell type that will eventually make the human heart. The embryonic stem cell (Es cell) and the EG cell embryonic germ cell (EG cell) are termed pluripotent-they have the ability to grow into several specific cell types, the cells that go ultimately to make the heart, those that make muscles and bones and so on. The attempt is to take the Es or EG cells and manipulate the conditions by growth in a manner that they will produce, say the heart tissue or the kidney tissue and so on.

Perhaps the most exciting thing that is going to happen in next three, four, five years is that you pickup appropriate cells, seed them right, make the organ of your choice and tissues from the embryonic stem cells, fortunately, would also be universally accepted. Even 4-5 weeks abortive tissue can be used, because human embryos and for that matter most animals at the embryonic stage are still what you call immuno-innocent. They do not have the ability to differentiate self from non self. Genetically engineered pigs or suitable breeds of pigs can be cloned for organ transplantation.

Population of endangered species of animals can be increased by cloning.

Cloning can be of immense use in improving the pedigree of live stock. Superior breeds of animals can be multiplied by this technique.

The scientists, have tried to focus public attention on the medical benefits that would result from cloning eg; in Scotland PPL. Therapeutics, owner of the rights of the sheep cloning, has developed a cow that produces milk containing human milk protein, useful to those babies who need mothers milk. The sheep experiements are part of effort to develop drugs for hemophillia and cystic fibrosis.

Cloning can eventually help to treat human brain damage.

Cloning is a common practice in Horticulture.

Days are not far off for a cloning laboratory to encounter a patient with a request to develop a clone for himself to circumvent any eventual (organ) kidney failure.

The debate on cloning has once again provided an opportunity where a scientific break through has stepped beyond traditional, legal, institutional and moral boundaries. Various countries have set up pannel of experts to review the implications of this new break through and suggest legal ways and means to prevent abuses. "You cannot blame scientists for making these kinds of discoveries—It is now upto society to decide how it should be used" otherwise the question "today the sheep, tomorrow the shepherd? is the clock tickling for a bilogical Hiroshima? will be in the minds of people, although perhaps not, because man is, after all, a rational creature and scientists are cautions.

References:

1. K.H.S. Campbell, J. Mcwhir, W.A. Ritchie and I. Wilmut Sheep cloned by nuclear transfer from a cultured cell line. Nature, Vol.380, 7 March 1996.
2. MC Grath,J and Solter, D. Science 220, 1300-1302 (1983).
3. Hooper, M.L. Embryonal Stem cells: Introducting planned changes into Germline (ed. Evans H.J.) (Harwood Academic, Switzerland 1992).
4. Campbell K.H.S. Ritchie WA, an Wilmut I. Biol Reprod 49, 933-942 (1993).
5. Campbell KHS, Loi P, Capai P and Wilmut I. Biol Reprod 50, 1385-1393 (1994).
6. Willadsen SM: Nature 320,63-65)1986).
7. Gerfen RW and Wheeler MW Anim Biotechno 6,1-14 (1995).
8. Malhotra A.M. Junior Science, Refresher - (May 1997); 7-9, 50.
9. Joshi P.C. Science Reporter. Feb. 1998; 19-23.

JK-PRACTITIONER

PATIENT SATISFACTION SURVEY OF EMERGENCY DEPARTMENT AT A LARGE TEACHING HOSPITAL

Syed Amin Tabish M.D.; Farhat Hussain Dawarki MD.

Abstract: *Quality improvement in hospitals requires effective measurement of patient satisfaction. Patients satisfaction information identifies areas of strength and weaknesses in the organization. Patient satisfaction is a signifcant issue for Emergency Departments. For many patients, the visit is their first to the particular Emergency Department. Morevoer, one-quarter to one-half of all inpatients are typically admitted through the Emergency Department. The special nature of the emergency encounter calls for a sound understanding of factors that have most influence on patient satisfaction. A study was conducted in the Emergency Department of a large teaching Hospital to determine the patient's perception of the care received by them in Emergency by analyzing the results of responses to a questionnaire and also to determine the relative importance of several components of patient satisfaction with services. The study revealed that personalized care rendered by doctors and paramedics, waiting time, public relations etc. are the key factors that drive satisfaction.*

Key words: *Hospital, emergency, Patient satisfaction.*

JK-Practitioner 1999; 6(3):247-249

Methodology

The study was performed at a teaching hospital. It has a well equipped and adequately staffed Emergency Department which provides round the clock services. Patients from all over the city and other districts come to this hosptial for care.

A structured interview schedule with alternative answers was evolved to ascertain the satisfication profile of patients attending the Emergency. Structured schedule was prepared that was simple to administer and less time consuming during the process of analysis. The interview schedule was pretested. The sample of interview was randomly selected and opinion of 100 patients was taken.

The respondents were assured and taken into confidence and were explained the objectives of the interview in order to elicit accurate responses.

Observation and Discussion

The responses of a sample of one hundred patients admitted in Accident & Emergency Services were obained in response to a simple structured questionnaire, regarding their satisfaction in relation to the services provided to them. The patients were interviewed in three different shifts: morning, evening and nights. 45% patients were admitted in the morning shift, 35% during evening and 20% patients during the night shift. 70% patients were present in Emergency Reception, 15% in Emergency Ward and 15% in Observation Ward, while recording their responses.

The age of the patients, whose responses were recorded, is shown in Table-1, which shows that the highest number of respondents were in the age group of (16-45) years i.e. 65% and the lowest number were aged between (6-15) years i.e. 7%. The distribution as per the sex of the patients shows that 68 (68%) were male and the remaining 32 (32%) were female patients. Regarding occupation of the respondents 30% patients were (male) Farmers and 29% (females) were house-wives.

Table-1: Demographic Data of Patients.

S.No.	Date		Percentage
01.	Age		
		0-5 years	0
		6-15 years	7
		16-45 years	65
		46-65 years	20
		65 + years	08
02.	Sex		
		Male	68
		Female	32
03.	Occupation		
		Farmer	30
		House-wife	29
		Labourer	15
		Student	12
		Service class	08
		Business class	06
04.	Hours of the Day		
		8-2 a.m.	45
		2-8 p.m.	35
		8-8 Night shift	20

From the Department of Hospital Administrate SKIMS, Soura, Srinagar India (Tabish, Dawarki)

Received January 1999 Accepted March 1999

Correspondence to : Dr. Syed A. Tabish, P.O.Box 826, GPO, Srinagar-190001

Table-2: Details of responses significantly correlated with respondent's satisfaction with outcome

S.No.	Questions and Responses	Total (in %)
01.	How long did you wait to be seen by the doctor	
	a. 0-15 minutes	78
	b. 15-30 minutes	6
	c. >30 minutes	16
02.	How long did you spend in the Emergency Deptt.	
	a. 0-1 hour	8
	b. 1-2 hours	6
	c. 2-3 hours	4
	d. 3-4 hours	2
	e. 4-5 hours	18
	f. 5-6 hours	12
	g. > 6 hours	50
03.	How long did you wait for treatment.	
	a. 0-30 minutes	94
	b. 30-60 minutes	2
	c. > 60 minutes	4
04.	Did the doctor explain what he was about to do	
	a. Yes	50
	b. No	38
	c. Vaguely	12
05.	Whether you were given adequate instructions about the follow up or not?	
	a. Yes	60
	b. No	40
06.	How was the behaviour of the staff	
	a. Helpful	76
	b. Not helpful	17
	c. Indifferent	7
07.	In your opinion the services were either	
	a. Prompt or	78
	b. Slow	22

Out of 100 patients, whose responses were recorded regarding the quality of services provided to them, 78% described it prompt service as they were attended within 15 minutes of reporting in Emergency Department. However, 6% had to wait for 15-30 minutes, and 16% of patients were attended after they waited for 30 minutes or more. 10% of patients attributed it to over crowding as they received the delayed attention due to the overbusy Emergency Reception area at that point of time, yet 9% blamed the staff for their apathy, for the same 45 blamed the management for the scarce staff or the bed strength.

The stay in the Emergency Department was more than 6 hours for 50% patients, 3-6 hours for 30% patients and 0-3 hours for the rest 20% patients. Half of the total number of patients needed a prolonged observation and others a short stay. Out of 50% patients who stayed for more than 6 hours 20% of such patients had to stay for more than 24 hours in Emergency Reception which was not as per the hospital policy. This was due to non-availability of beds in respective specialities where they were supposed to be transferred after 24 hours as a routine practice.

Within first 30 minutes 94% patients were given the required treatment and they described it as on time medical care provided, while 2% got the same within 30-60 minutes and 4% got it after one hour. 6% were dissatisfied due to delayed medical care provided to them.

50% of patients were explained what needs to be done or what is the aliment like and were satisfied but 38% were not explained their problem. 12% were vaguely infromed in this regard.

60% patients were not instructed about the follow-up and were not aware about the continuity of treatment after getting discharged while 40% knew even the days of the week (when to report) after getting discharged from the hospital.

The receptionist and the medical record technician have been very helpful in 83% cases, who needed guidance and 27% knew to whom to report or how to proceed. Their behaviour has been rated good (Table-3).

Co-operation by the supportive staff in majority of patients have been very satisfactory and their skill also appreciated (92%), while in 8% this was not satisfactory. Majority of patients (76%) were satisfied with the behaviour of the staff and labeled them courteous and helpful. 24% narrated unsatisfactory behaviour. Although 4% related it to overcrowding of patients yet the rest 20% described it as the indifferent attitude of the staff.

Overcrowding observed by the majority of patients (92%) is attributed to the indiscipline by the public and carelessness on the part of staff who are supposed to regulate the rush of patients. They attribute it to the inconvenience to the public as well as the staff. Supportive staff like sanitation also had to put efforts to maintain the cleanliness and hygiene of Emergency Department.

Only 12% patients mentioned that doctor was interrupted while examining a patient and they attributed it to the apprehensive patients, their attendants and overcrowding.

56% patients said that the Emergency Department was half-full at the time of reporting of patient to the doctor, 36% described it full and the rest 8% labeled it empty area when they reported first.

92% patients said that the staff was skillful including that of supportive services i.e. (ECG, X-ray and a Laboratory person) but 8% were not satisfied.

Table-3: Details of responses not significantly correlated with respondents satisfaction with outcome

S.No.	Questions and Responses	Total (in %)
1.	Was the receptionist helpful	
	a. Yes	73
	b. No	27
2.	At the time you arrived in Emergency reception, was it	
	a. Empty	8
	b. Half-full	36
	c. Full	56
3.	Whether the department was busy when you reported first	
	a. Yes	92
	b. No	8
4.	Was the doctor interrupted while examining the patient	
	a. Yes	12
	b. No	88
5.	Technical skills of the Nursing staff	
	a. Excellent	0
	b. Good	10
	c. Satisfactory	90
	d. Unsatisfactory	0
6.	Doctor explains the results of investigations done or not	
	a. Yes	80
	b. No.	20
7.	Courtesy of the doctor	
	a. Yes	88
	b. No	12
8.	Courtesy and Co-operation of supportive staff	
	a. Yes	92
	b. No.	8

80% patients said that doctors explained the tests done on the patients and their results, while 20% patients said that doctors did not bother to explain such important interventions.

Regarding the suggestions of the respondents patients did not speak enough except that they wanted prompt and proper treatment and cordial attitude of the staff.

Conclusion

Although majority of patients were satisfied with the services provided to them, yet some aspects of patient care were neglected and lot of improvement can be achieved further. These aspects include:

The patients who had to wait for getting treatment must be promptly attended. This aspect pertains to the nursing care who must be made aware of this kind of service and the problems which they face must be looked into in time.

Technical skills of the staff involved in providing the services has been found satisfactory including those of supportive services.

The staff must be more concerned about the promptness of the treatment to be provided as the patient's ailments are of emergent nature.

Doctors need to inculcate the habit of explaining the problem, the investigations and regarding followup so that patients take appropriate care of their problem and are well informed. Traffic of patients must be regulated properly and overcrowding avoided. Proper shifting of patients as per the schedule must be implemented so that enough beds are available for the patients who report.

The study revealed that personalized care rendered by doctors, nurses and paramedics and waiting time are the key factors that drive satisfaction with emergency department.

References:

1. Tabish A. Patient focused Emergency Department. Journal of Medical Sciences 1998; 1: 6-9.
2. Clearly PD and BJ McNeil. Patient satisfaction as an indicator of quality care. Inquiry 1988; 25: 25-36.
3. Kathryn H Dansky and Diane Brannon. Discrimnant Analysis. A technique for adding value to patient satisfaction surveys. Hospital and Health Services Admn. 1996; 41: 503-513.
4. Melvin F Hall - Keys to patient satisfaction in the Emergency Department: Results of a Multiple Facility Study. Hospital & Health Services Admn. 1996; 41: 515-532.

"ALL EXCEPT"

1. The contralateral side of the body has strict topographical represenation in the cerebral cortex except Olfactory system which has no cortical representation.
2. All the sensory systems have descending fibres for mudulation and feed back control of information except olfactory system which does not project back.
3. Descending fibres are not very prominent except auditory system where they arise from the auditory cortex, the inferior colliculi and the superior olivary complex and pass to the receptor cells from the superior olivary complex.
4. No glands develope from the neural crest except adrenal medulla. Here the mirgrated neural crest cells differentiate into secretory cells instead of ganglion cells and receive preganglionic autonomic fibres with norepinephrine as the mediator.
5. All the cardiac branches of Vagus and sympathetic contain both afferent and efferent firbres excet cadiac branches of superior cervical sympathetic ganglion which is purely efferent.
6. Preferential thoroughfare channels resemble typical capillaries in structure except that the widely spared smooth muscle fibres in the well spiral around the endothelium and the calibre of this capillary is larger.
7. Superior vena cava drains venous blood above the umbilicus except he lungs.
8. A. Oesophagus is related to the mediastinal pleura on the right side except where azygos vein passes from posterior to the anterior end.

   B. The left side is close to the mediatinal pleura except where thoracic duct and left subclavian artery intervene.

   (These relations have developed more importance recently while choice of resection of parts of oesophagus is resortted in various surgical problems.)
9. Azygos vein drains all the posterior intercostal veins except the upper two.
10. All the ribs articulate with two demifacets of adjoining vertebrae except the first and last three.
11. All the ribs form costotranverse joints except the 11th and the 12th.
12. All the sternocostal joints are synovial except first which forms synchondrosis.
13. All the interchondral joints are plane synovial joints except the joint between 9th and 10th costal cartilages which is a fibrous joint.
14. All the vessels arising from the heart have tunica media of elastic nature except ductus arteriosus which is muscular. Its constriction starts after birth when the PCO_2 of the blood flowing through it reaches 50mm Hg.
15. The nerve fibres in unmyelinated nerves lies in the cytoplasmic invagidnation of the Schwann cell—one fibres in one invagination except in olfactory nerves where multiple (May be 20) axons occupy each invagination.
16. Neurons have axons and dendfrites except amacrine cells in the retina and granule cells in the olfactory bulb which have no axons.
17. Myelinated nerve fibres are ensheathed by cytoplasm of the Schwann cell except at the terminal and the initial segment. (Teloglial cells are found in relation with the terminal parts of the nerve fibres.)
18. The major sensory and dmotor pathways send fibres often as collaterals to the reticular formation except medial lemniscus which does not send collaterals.
19. Epithelial cells (membrane) usually restraction on one basal lamina even when it stratifies during devlopment except neuroectoderm where the tall columnar or cuboidal neuroectodermal layer (which is the precursor of the mantle and marginal layers) lies between two limiting membranes-one on the luminal (Spinal or central canal) side and the other on the deeper side (the side which adjmins later in development as the intermediate MANTLE layer for this EPENDYMAL layer).
20. Capillaries open into the venules randomly without any angultion (Definite angulation) except in the germinal matrix of brain (It is the border zone between cerebral arteries and the collection zone of deep cerebral veins) where the capillaries open into the veins directly at right angles (These vessels may be the points of vascular rupture and the sites of subpendym
21. All the veins have got valves within these except Cerebral, Vertebral, portal and those within the bone marrow.

Dr. Abdul Ahad Deptt. of Anotomy, GMC, Srinagar

THE ELECTRONIC HIGHWAY IN MEDICINE

S.A. Tabish M.D.

Health care is the largest industry in the world and its sheer size and complexity makes change an evolution of mammoth proportions. In recent years, however, global pressures of increasing and aging populations, new ailments and more complex and advanced treatments have put pressure on health systems to look at ways of controlling costs.

Today's challenging healthcare environment demands that hospitals and health systems continuously monitor, improve and refine how they deliver patient care efficiently. One of the most important criteria for delivering effective and efficient healthcare is seamless communication between hospital employees, departments and facilities in real time. And, while the challenge of integrating information between people, places and things may seem daunting, technological advances have made its possible and are helping organisations improve the value of the care they deliver.

Information systems in healthcare industry have been in practice for many years. Traditionally used for patient administration or financial applications, these systems provided benefits to the administrative side of healthcare organisations, but did little to impact on patient care or clinical practice. As healthcare software advanced through the decades, applications for laboratory, radiology, pharmacy and nursing were implemented to assist professionals in these departments and these began the basis for an electronic medical record.

Clinical information management for image and data sharing is becoming the next stage in the evolution of the trend towards multimedia medicine.

With the advent of the Internet, patients are becoming more informed and better consumers of the health care industry. They are demanding earlier diagnosis, faster treatment and interventions based on evidence, not traditional practice. Healthcare organisations and practitioners faced with these demands and the need to control spiraling costs have looked for ways to deliver care in more efficient ways, places and time.

Through the Internet, the public has access to growing supply of information on health and disease, often of variable quality and relevance. As a result, providing information on health will no longer be the exclusive remit of health care professionals. The quantity of the information on the Internet will continue to grow over the next few years, as will the proportion of people with access to it.

Healthcare information on the Internet has potential benefits for the patients. Numerous electronic discussion groups already allow patients to share experiences and some health related Internet sites offer email advice on a fee for service basis.

The Internet is the largest computer network in the world. It is also a virtual community. Almost any type of computer can connect to it. The benefits to medical practitioners of using the Internet are growing rapidly. Much of the recent interest in the Internet centres on a relatively new features, the world wide web (the WWW or the Web). This provides a user friendly method for accessing, manipulalting, or even publishing information on the Internet.

Electronic mail (E-mail) has many advantages over other forms of communication: it is easy to use, relatively free of charge, fast, and delivers information in a digital format. Email is the transmission of text messages between networked computers.

The world wide web provides a uniform, user friendly interface to the Internet. Web pages can contain text and pictures and are interconnected by hypertext links. Programmes that allow you to use the web are available for most operating systems. Powerful on line search engines make it relatively easy to find information on the web.

The Internet is accessible from most parts of the globe, and access and dissemination is largely uncontrolled. The quality of information varies widely, from the most upto date practice guidelines produced by leading clinical bodies to out of date or inaccurate recommendations. In countries where patients can participate in the choice of treatment the Internet could potentially be rich source of information on treatment options, but meeting patient's expectations and managing their requests presents an important challenge for providers of healthcare.

In countries in which health care is more centrally managed, wide spread use of the Internet is likely to aggravate existing conflicts between patients expectations and provision of health care.

In providing information on which to base best practice, bodies like the Cochrane Collaboration have become pivotal, as has the development of clinical tools for rapid and accurate access to such information across the Internet. Pooled practice guidelines will be a resource not only for doctors but, in all probability, for patients as well.

Delivering health care has several basic requirements that must be met in order for the clinician to support the implementation of healthcare information technology:

- Data collection
- Data review and acknowledgment
- Documentation of a Plan of care.
- Management of the Plan of care.

The right kind of information technology system can play an important role in assisting medical staff in delivering care. The commitment must be to improve clinical work flow.

Innovative approaches to scientific publishing may make it possible to use the Internet itself to redress the mismatch in the speed with which new scientific results can be disseminated and the length of time required for careful peer review. It should at least be possible to provide guidance for internet users on the best available sources of healthcare material.

The changing nature of the information delivery brings with it enormous implications for the delivery of healthcare.

The best way to address the issues of cost, quality, access and evidence - based care is through the right information, in the right place, at the right time information that provides the complete picture so that a physician has all the evidence to make a correct diagnosis. The key to multimedia medical environment is integration and availability. This needs systems and networks designed for high availability with a solution partner specialising in seeing the big picture in providing and integrating PACS (Picture archiving communication system) and telelmedicine solution with the leading healthcare information systems.

Syed Amin Tabish
Associate Professor
Deptt. of Hospital Administration
SKI Institute of Medical Sciences
Srinagar, Kashmir
JK-Practitioner 1999;6(4): 251-252

Further Reading:

1. Bob Iocona. Multimed Medicine - Seeing the big picture in Health care. Hospital Management International 1999;73.
2. Mark Pallen. Introducing the Internet. BMJ 1995;311:1422-4.
3. Mark Pallen. Electronic mail. BMJ 1995;311:1947-90.
4. Mark Pallen. The World Wide Web. BMJ 1995;311:1522-6.
5. Tom Jones. Improving clinical work flow. Hospital Management International, 1999;69.

DECLARATION UNDER SECTION 5 OF THE PRESS AND REGISTRATION BOOKS ACT OF 1967 AS AMENDED FROM - (SEE RULE I)

1.	Title	**JK - PRACTITIONER**
2.	Place of publication	Srinagar
3.	Periodicity of publication	Quarterly
4.	Publisher's name	Dr. G. M. Malik
	Whether Citizen of India	Yes
	Address:	Jhelum Market, Batamaloo, Srinagar - 190 010, Kashmir (India)
6.	Citizen of India	Yes
	Address	Jhelum Market, Batamaloo, Srinagar - 190 010, Kashmir (India)

7. Particulars of other individuals who are owners/shareholders of Newspaper.

I Dr. G. M. Malik hereby declare that the particulars given above, are true to the best of my knowledge and belief.

sd/-
Dr. G. M. Malik

ADVANCES IN DRUG TREATMENT OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING

M S Khuroo MD, DM, FACP, FRCP (Edin), Naira S. Khuroo MBBS

Upper gastrointestinal bleeding is an important cause of hospital admissions and mortality. It is estimated that upper gastrointestinal bleeding results in around 300,000 hospital admissions in the United States and around 25,000 hospital admissions in British hospitals annually. During the past fifty years, the morbidity and mortality from upper gastrointestinal bleeding has remained unchanged at around ten percent, despite improved medical and surgical treatments, the emergence of endoscopy and endoscopic therapy in the diagnosis and therapy respectively and the availability of intensive care units[1].

Etiology: The most common causes of upper gastrointestinal bleeding is peptic ulcer, with gastric and duodenal ulcer each accounting for about 20 to 25% of all episodes[2]. Gastritis, mostly related to drugs and alcohol, accounts for 20 to 25% of episodes of upper gastrointestinal bleeding. Hemorrhagic gastritis as a result of sevre underlying illness (i.e., "stress gastritis" in the face of sepsis, burns, shock, post-operative states, respiratory failure, etc.) is a problem primarily of patients already hospitalized for other rasons. Bleeding from esophageal or gastric varices account for 10 to 20% patients of upper gastointestinal bleeding and Mallory-Weiss tears in around 7% Multiple etiologies are found at endoscopy in up to 30% of patients. The list of rare or less frequently diagnosed causes of upper astrointestinal bleeding is extensive[3,4]. In addition, all studies include a proportion of cases with no identifiable bleeding source at endoscopy.

Management: the key to management of patients with upper gastrointestinal bleeding is adequate initial and ongoing assessment and resuscitation[5]. Fortunately, the bleeding stops spontaneously in around 70 to 80 percent of patients and such patients can be discharged from the hospital within 24 hours. Early endoscopic examination is essential to detect patients with continued bleeding or those with high risk of rebleeding. Endoscopic intervention is effective and beneficial in such patients. Surgery is reserved for patients with failure to endoscopic therapy[6]. Assessment of presence and severity of co-morbid diseases have a great impact to the overall prognosis and shall determine the level of medical care to be delivered. Medical therapy including gastric lavage and antacids are of unproven value in the management of upper gastrointestinal bleeding.[7]

Drug therapy versus interventional treatment: Durg therapy for upper gastrointestinal bleeding is an attractive option with many distrinct advantages[8]. The most important advantage of drug therapy over endoscopic treatment is its wide application. Recent data regarding the outcome of endoscopic management have been derived from randomized controlled trials at reserarch institutions with high procedure volumes and expert endoscopists. A recent assessment of the impact of endoscopic therapy in general US population showed that endoscopy was performed on only 57 percent of patients with ulcer bleed and therapeutic endoscopy was performed in only 13 percent of patients. 6.1 percent of patients underwent surgery, of these 74 percent had no attempt at therapeutic procedure[9]. In addition, majority of patients with upper gastrointestinal bleeding will initially be cared for in general hospitals, which may lack the endoscopy facilities and skilled endoscopist. Drug therapy that may stop bleeding can buy time to allow a skilled endoscopist to be called in or to failitate safe transfer. Use of drug therapy during resuscitation or at home or during transfer to hospital are other potential advantages over endoscopic treatment.

H_2 receptor antagonists, Tranexemic acid and Somatostain: H_2 receptor antagonists are widely employed in the therapy of upper gastrointestinal bleeding. To date, no study has conclusively shown that such therapy is of value in stopping bleeding or improving outcome of patients with upper gastrointestinal bleeding. Zuckerman et al studied the role of cimetidine in 285 patients with active bleeding and in another 194 patients of upper gastrointestinal bleeding who had stopped the active bleeding[10]. Cimetidine 300 mg or a placebo was administered intravenously every 6 hours to patients with upper gastrointestinal bleeding caused by endoscopically

---

JK Practitioner 199;6(4): 253-258
From Deptt. of Medicine, King Faisal Specialist Hospital & Research Sciences, Gastroentrology Section Saudi Arabia (Prof M S Khuroo) and JVMC, Srinagar Kashmir (Naira) Received : August 1999 Accepted September 1999

confirmed peptic ulcers, gastric erosions, varices and Mallory-Weiss tears. There was no significant difference noted between cimetidine and placebo group in stopping active bleeding (71% vs. 77%) or in reducing rebleeding episodes (24% vs. 26%). Evaluation of specific bleeding and the prevention of recurrent bleeding during a single hospitalization appeared to be unaffected by therapy with H_2 receptor anatagnoists. Collins and Langman examined the data of 27 available randomized trials, in which over 2500 patients were entered[11]. This mata-analysis suggested that treatment with H_2 receptor antagonists might reduce the rates of rebleeding, surgery and death by 10, 20 and 30 percent, respectively, although these results were marginally significant for surgery and death. Any benefit appeared to be confined to patients with bleeding gastric ulcers. The authors concluded that treatment with H_2 receptor antagonists was moderately promising and called for further large-scale studies. Such a study was performed comparing intravenous famotidine with placebo in 1005 patients with peptic ulcer bleeding and stigmata of recent hemorrhage[12]. Case fatality, rebleeding and surgery rates were not different between the two groups. It was concluded that H2 - receptor antagonists did not influence the natural history of peptic ulcer bleeding.

Barer et al studied the effects of tranexamic acid and cimetidine on 775 patients with upper gastrointestinal bleeding in a double blind randomized placebo-controlled trial[13]. Tranexamic acid and cimetidine were not associated with decrease in rate of rebleeding or need for surgery, however, mortality was significantly reduced in patients receiving tranexamic acid (6.3%) and cimetidine (7.7%) when compared to those with placebo group (13.5%). As there were disparate trends in mortality and severity of bleeding, authors suspected that reduction in mortality could have arisen by chance and may not represent the drug effect.

In another double blind placebo-controlled multicenter trial in 23 German centers, somatostain analogue, octerotide, resulted in no difference in stopping bleeding and preventing rebleeding when compared to placebo[14]. Surgery rates, blood transfusion requirement, and time required before bleeding stopped were not different between two groups. A retrospective analysis did not identify a subgroup of patients, which might have benefited from the analogue. In an editorial in Gastroenterology on this study, Peterson et al likened the quest of pharmacotherapy of peptic ulcer bleeding to search for the Holy Grail and recommended that it was time to give up the search[15].

Pathogenesis of bleeding vessel: Pharmacotherapy of peptic ulcer bleeding has been revolutionized by the understanding the pathogenesis of bleeding lesion in major peptic ulcer bleeds[16]. Major bleeding from peptic ulcer is arterial in origin. As the name suggests, the visible vessel was originally thought to represent the bleeding artery itself. However, pathologic analysis disclosed that the protuberance was actually an organized clot plugging a side hole in the bleeding artery located just beneath the ulcer base. A sentinel clot (visible vessel) plugs the bleeding point, which initially is contiguous with a larger overlying clot that eventually falls off. At first the sentinel clot is fresh red in color, but it darkens with time as the hemoglobin changes color. Later the red blood cells are lysed, leaving a white plug of fibrin and platelets. Eventually, the raised plug disappears as the healing process is completed. Second look endoscopy in peptic ulcer bleeds has shown that rebleeding is result of breakdown or dissolution of the sentinel clot and stability of sentinel clot and its evolutionary changes as mentioned above prevent rebleeding. The main way to control peptic ulcer bleeding would be to stabilize the sentinel clot during immediate post bleeding period and few days following bleeding.

Berstad et al performed a simple in vitro experiment by observing percent digestion of a well retracted clot plotted against time when placed either in diluted gastric juice or in a similar concentration of diluted hydrochloric acid[17]. The clot placed in gastric juice was digested within minutes, whereas the clot placed in a similar concentration of acid stays intact during similar period. Proteo-fibrino-lysis by pepsin is therefore a possible mechanism by which the sentinel clot can be removed and rebleeding is provoked.

How can peptic activity in the gastric juice be inhibited early in the course of gastrointestinal bleeding and the sentinel clot prevented from digestion? Recently Patchett and O'Donoghue (1995) used thrombelastography to determine the effects of pharmacological manipulation of gastric juice on coagulation and fibrinolysis[18]. They showed that gastric juice causes both significant impairment of clot formation and accelerates lysis of a formed fibrin clot. Both clot formation and clot lysis are likely to be of clinical relevance in a patient with an upper gastrointestinal bleeding. Acid neutralization was clearly of benefit in optimizing clot formation and in preventing fibrinolysis. This supported the hypothesis that profound acid suppression such as that with agents such as Omeprazole may have a part to play in the setting of peptic ulcer bleeding. Agents such as sucralfate, aprotinin, and tranexamic acid would seem to be less appropriate on the basis of this work. These agents reduce clot lysis but their adverse effects on the dynamics of cloth formation show that their use in active bleeding may not ideal.

Acid neutralization and sentinel clot: Next to define was how could acid secretion be reduced or acid neutralization doe in the setting of acute gastrointestinal bleeding so that peptic activity be inhibited and setting a stage for sentinel clot stabilization? We performed experiments with intragastric pH studies in patients with upper gastrointestinal bleeding and depicted 24 hours intragastric median pH values every 10 minutes periods on 10 randomly selected patients[19]. None of the patients was actively bleeding at the time of intragastric pH studies. 5 patients received Omeprazole 80 mg administered orally in two divided doses and another 5 patients received identical looking placebo. The pH values were recorded on the second day of drug therapy. The median pH values in the placebo group remained in the acidic range (pH 0.7-3.5) compared Omeprazole group in whom the pH values ranged from 5.9 to 7.2. All the median pH readings on the placebo were below 3.5, while all median pH readings in the Omeprazole group were above 5.9. In fact 98% of pH readings in patients on Omeprazole were above 6.8. All median pH values recorded over identical time periods between Omeprazole and placebo groups differed significantly from each other. We concluded that omeprazole in the dose given could bring the gastric pH values to the level that peptic activity may be inhibited.

What about H-2 receptor antagonists? Lanas et al recorded continuous 24 hour intrgastric pH in 20 patients with bleeding doudenal ulcer who were not actively bleeding at the time of examination[20]. Ten patients received omeprazole 80mg followed by 40mg 12 hourly intravenously and other 10 patient received ranitidine 50mg 4 hourly intravenously (300mg/day). At these doses ranitidine was significantly less effective than omeprazole in keeping the intragastric pH above the proteolytic range for pepsin. The percentage of time the gastric pH was <6 in omeprazole treated patients was 15.3% vs. 61.8% in those treated by ranitidine. The difference was highly significant. Also the number of times the pH was <6 for >5 minutes was 12 in ranitidine group vs. 3.4 in omeprazole group, the difference being again significant. The authors concluded that omeprazole might have a beneficial therapeutic effect on the outcome of peptic ulcer bleeding. In another study Lin et al recorded intragastric pH at 6-second intervals for 24 hours in 50 patients with upper gastrointestinal bleeding treated with Omeprazole 40 mg bolus followed by a 160 mg continuous infusion daily for 3 days and in another 50 patients with upper gastrointestinal bleeding treated with Cimetidine 300 mg bolus followed by 1200 mg continuous infusion daily for 3 days[21]. The mean intragastric pH rose to 6.0 one hour after the initial bolus of Omeprazole in the Omeprazole group; it persisted around this value for the rest of the 24 hours. In the Cimetidine group, the mean intragastric pH rose to 4.0 one hour after the initial bolus of Cimetidine and persisted around 4.5 to 5.5. for the rest of the 24 hours. The duration in time of the raised intragastric pH (>6.0) was 84.4% in the Omeprazole group, compared with 53.3% in the Cimetidine group. The difference was statistically significant.

Omeprazole and peptic ulcer bleeding: In 1997, three double blind placebo controlled trials were published on the role of omeprazole in patients with bleeding peptic ulcers and stigmata of recent hemorrhage[19,22,23]. All the 3 trials though differing in design came to the same conclusions. Omeprazole was found beneficial in peptic ulcer bleeding with stigmata of recent hemorrhage.

We reported the results of a double-blind, placebo-controlled trial of oral omeprazole (80 mg in patients with endoscopically confirmed peptic ulcer bleeding with stigmata of recent hemorrhage[19]. None the patients had received prior therapeutic endoscopic treatment. Over a 2 year study period, 542 of the 869 patient with upper gastrointestinal bleeding had peptic ulcers at endoscopy. 220 of the peptic ulcer patients had stigmata of recent hemorrhage and were randomly distributed into omeprazole and placebo group. Twelve of the 110 patients treated with omeprazole (10.9 percent) had continued bleeding or further bleeding compared with 40 of the 110 patients who received placebo (36.4 percent). Eight patients in omeprazole group and 26 patients in the placebo group required surgery to control their bleeding. The differences in rate of further bleeding and surgery were highly significant ($p<0.001$). Two patients in omeprazole and six in the placebo group died a difference that was not significant with corresponding death rates of 1.8 percent versus 5.4 percent respectively. Subgroup analysis showed that omeprazole was associated with significant reductions in recurrent bleeding in patients with non-bleeding visible vessels or adherent clots and not in those with arterial spurting or ozing.

Two European multicenteric trials used omeprazole 80 mg administered as in intravenous bolus followed by omeprazole intravenous infusion 8 mg per hour for 72 hours. In the report by Hasselgren et al, 333 patients ≥60 years old with peptic ulcer bleeding and stigmata of recent hemorrhage were recruited from 20 centers in Sweden and 9 centers inNorway[22]. Endoscopic treatment was allowed only in patients with spurting bleeding. Omeprazole reduced the need for blood transfusions, surgery, and endoscopic treatment and subsequently improved overall outcome in peptic ulcer bleeding, when assessed at 3 days and 4 to 21 days duration. The mortality in placebo patients was extremely low, one patient died (0.6%), while 11 omeprazole patiets (6.9%) died, which was within expected range. In another trial, Schaffalitzky et al recruited 274 patients from 34 hospitals in Denmark, Holland and France[23]. Endoscopic treatment was allowed in all patients with stigmata of hemorrhage. Omeprazole significantly reduced the number of operations, endoscopic treatment and duration and severity of bleeding, when assessed at 3 days and 4 to 21 days duration.

From the above published trials it could safely be concluded that Omeprazole is found beneficial in peptic ulcer bleeding with stigmata of recent hemorrhage[24,25,26]. The benefit was limited to subgroup of patients with visible vessel or clot and not in those with spurting or oozing. The benefit achieved was in rebleeding rate, transfusion requirement and rate of surgery. Two studies showed a trend towards improved survival in favour of omeprazole, however, the values did not reach statistical significance. The obvious advantages of use of drug therapy in ulcer bleeding namely use of omeprazole at home, during transfer or in the emergency room setting during resuscitation need future studies.

Recently medical treatment of bleeding peptic ulcer has also been focussed at prevention of rebleeding after the initial hospitalization over next one to two years. Data from number of studies involving a limited numbr of patients showed that long term rates of rebleeding in patients treated for Helicobacter pylori significantly lower than those not treated. Thus it would seem wise as ever to treat all patients of bleeding peptic ulcer for Helicobacter pylori to prevent ulcer recurrences and rebleeding.[27]

NSAID and gastrointestinal bleeding: About 30 million people worldwide use non-steriod anit-inflammatory drugs and over 10 percent of these are over 60 years of age. Non-steriod anti-inflammatory drugs account for over twenty percent of all drug reactions and such reactions account for seventy thousand admissions and seven thousand deaths in United States per year. Ten to forty percent of patients on long term use of non-steriod anti-inflammatory drugs develop gastrointestinal symptoms, ten percent develop peptic ulcer and 3 percent have serious complications like gastrointestinal bleeding and/or gut perforation[28].

Pathogenesis of gastrointestinal injury by non-steroid anti-inflammatory drugs is now better understood. These agents deplete the prostaglandin from the gastric and duodenal mucosa, thereby reducing the production o mucus and bicarbonate, and impair mucosal blood flow. This pathogenic factor has formed the basis of misoprostol therapy. The discovery of COX-I (cyclo-oxygenase-I) and COX-II (Cyclo-oxygenase-II) shall lead to a major impact of use of NSAID's in clincial medicine. COX-I is present in all tissues and mediates vascular blood flow and it seems to be the cause of NSAID induced side effects; COX-II is pro-inflammatory and normally only found at sites of active inflammation, in the central nervous system and kidney. Inhibition of COX-II seems to be responsible for the therapeutic effects of NSAIDs. If COX-I is inhibited then mucosal injury is initiated; this does not seem to happen when COX-II is inhibited. Selective COX-II inhibitor class of NSAIDs are already available and their use shall reduce gastro-intestinal and renal side effects, while maintaining anti-inflammatory effects of NSAIDs.[29,30]

Recent data have shown that acid and pepsin has a very important part to play in determining the severity of mucosal injury by the non-steroidal anti-inflammatory drugs. Acid has also an important permissive role in NSAID associated mucosal injury. Most NSAIDs are weak acids that selectively concentrate in the mucoa at low intragastric pH. This has formed the basis of treatment of NSAID-associated mucosal injury by H-2 receptor antagonists. However, concurrent use of NSAIDs slows the ulcer-healing rate achieved hitherto with H-2 receptor antagonists. This is a big limitation, as many patients on NSAIDs therapy have to continue the drug inspite of gastro-duodenal erosions or ulcers.

Recent data have shown that profound acid suppression induced by proton pump inhibitors markedly reduce NSAIDs and H-2 receptor antagonists. The data published by "Omeprazole verus Misoprostol for NSAID-Induced Ulcer Management" (OMNIUM) study group showed that in patients who required continuous NSAIDs and who had ulcers or erosions, omeprazole 20 mg had distinct therapeutic benefits over ranitidine and misoprostol. Omeprazole healed and prevented ulcers more often than ranitidine. Omeprazole was as efective as misoprostol in overall healing of ulcers, erosions and symptoms associated with NSAIDs. Omeprazole healed gastric and duodenal ulcers more often than misoprostol, whereas misoprostol healed erosions more often than was the fact that omeprazole was better tolerated than misoprostol[31,32]

This makes a strong case for use of omeprazole in patients with NSAID-associated injury, requiring continuity of NSAIDs. Which patients need long term prophylaxis is a matter of debate and to be seen from the purview of risk of gastro-duodenal injury and cost effectiveness and safety of long term drug therapy. A number of risk factors for gastro-intestinal complications have been identified including age over 60 years, history of peptic ulcer, male gender, alcohol intake, smoking and concurrent use of anticoagulants and corticosteroids. Out of these, prior history of peptic ulcer is the most important risk factor. It is strongly recommended that patients with three or more than three risk factors should receive prophylactic therapy[31,32].

Stress ulcer: Critically ill patients who require mechanical ventilation are at increased risk for gastrointestinal bleeding 33. There are conflicting data on the efect of H2 receptor antagonists and the cytoprotective agent sucralfate on the rates of gastrointestinal bleeding, ventilator-associated pneumonia, and mortality. In a multicenter, randomized, blinded, placebo-controlled study enrollig 1200 patients, Cook et al showed that ranitidine significantly lowered rate of clinically important gastrointestinal bleeding when compared to sucralfate, without any increase in ventilator - associated penumonia, hospital stay or mortality[34].

References:

1. Gilbert DA. Epidemiology of upper gastrointestinal bleeding. Gastrointest Endosc 1990;36: Suppl: S8-S13.
2. Gilbert DA, Silverstein FE, Tedeso FJ, Buenger NK, Persing J, and 277 members of the ASGE. The national ASGE survey on upper gastrointestinal bleeding iii. Endoscopy in upper gastrointestinal bleeding. Gastointest Endos 1'981;27:94-102.
3. Brauch EJ, Sivak MV, Sullivan BH. Aorto-duodenal fistula:Endoscopic diagnosis. Dig Dis Sci 1979;24:940-3.
4. Veldhuyzen Van Zaten SJO, Bartelsman JFWM, Schipper MEI, Tytgat GNJ. Recurrent massive hematemesis from Dieulafoy's vascular malformations-a review of 101 cases. Gut 1986;27:213-22.
5. Liebeman D. Gastrointestinal bleeding: initial management. Gastrintest Clinic North Am 1993;22:723-36.
6. Castell DO, Bozymski EM, Bulkley GB et al. Consensus conference -Therapeutic endoscopy and bleeding ulcers. JAMA 1989;262:1369-72.
7. Yavoherski RH, Wong RKH, Maydonovitch C, Battin LS, Furnia A and Amundson DE. Analysis of 3294 Cases of Upper Gastrointestinal Bleeding in Military Medical Facilities. Am J Gastroenterol 1995;90:568-73.
8. Langman MJS. Problems in assessing pharmacological treatment of acute upper gatrointestinal bleeding. Hepato-gastroenerol 1990;37:29-30. (suppl. 1).
9. Mallery S, Metfessel B, Freeman ML. Outcomes of therapy for bleeding peptic ulcers in the general U.S. medical community Am J Gastrenterol 1996;91:1919.
10. Zuckerman G, VWelch R, Douglas A, Troxell R, Lorber S, Melnyk C, Bliss C et al. Controlled trial of medical therapy for active gastrointestinal bleeding and prevention of rebleeding. Am J Med 1984;76:361-6.
11. Collins R and Langsman M. Treatment with Histamine H2 antagonists in acute upper gastrointestinal hemorrhage-implications of randomized trials. N Engl J MEd 1985;313:660-6.
12. Walt RP, Cotterll J, Mann SG, Freemantle NP and Langman MJ. Continuous intravenous famotidine for hemorrhage from peptic ulcer. Lancet 1992;340:1058-62.
13. Barer D, Ogilvie A, Henry D, Dronfield M, Coggen D, French S, Ellis S, et al. Cimetidine and tranesxamic acid in the treatment of acute upper of acute upper gastrointestinal tract bleeding. N Engl J Med 1983;308:1571-5.
14. Christiasen J, Ottenjann R, Arx FV an'the study group. Placebo-controlled trial with the somatostatin analogue SMS 201-995 in peptic ulcer bleeding. Gastroenterology 1989;97:568-74.
15. Peterson WL. Pharmacotherapy of bleeding peptic ulcer-is it time to give up the search? (Gastroenterology 1989;97:786-7.
16. Swain CP, Storey DW, Bown SG, Heath J, Mills TN, Salmon PR, Northfield TC, et al. Nature of the bleeding vessel in recurrently bleeding gastric ulcers. Gastroenterology 1986;90:595-608.
17. Berstad A. Does profound acid inhibion improve haemostasis in peptic ulcer bleeding? Scand J Gastrenterol 1997;32:396-8.
18. Patchett SE, O'Donghue DP. Pharmacological manipulation of gastric juice: thrombelastographic assessment and implications for treatment of gastrointestinal hemorrhage. Gut 1995;36:358-62.
19. Khuroo MS, Yatoo GN, Javid G, Khan BA, Shah AA, Gulzar GM, Sodi JS. A comparison of omeprazole and placebo for bleeding peptic ulcer. N Engl J Med 1997;336:1054-8.
20. Lanas A, Artal A, Blas JM et al. Effect of parenteral omeprazole and ranitidine on gastric pH and the outcome of bleeding peptic ulcer. J Clith Gastroenterol 1995;21:103-6.
21. Lin H, Lo W, Lee F, Perng C, Tsseng G. A prospective randomized comparative trial showing that omeprazole prevents rebleeding in patients with bleeding peptic ulcer after successful endoscopic therapy. Arch Intern Med 1998;158:54-8.
22. Hasselgren G, Lind T, Lundell L et al. Continuous intrenou infusion of omeprazole in elderly patients with peptic ulcer bleeding Scan J Gastroenterol 1997;32:328-33.
23. Schaffalitzky OB, Havelund T, Harling H, Boesby S, Snel P, Vreeburg EM, Erinksson S, et al. Eeffect of omeprazole on the outcome of endoscopically treated bleeding peptic ulcerss. Scand J Gastroenterol 1997;32:320-7.
24. Saltzman JR and Zawacki JK. Therapy for bleeding peptic ulcers. N engl J Med 1997;336:1901-3.
25. Peterson WL and Cook DJ. Antisecretory therapy for bleeding peptic ulcer. JAMA 1998;280:35-6.
26. Pedersen PJ, Bjorkman DJ. World literature review-comment. Am J Gastroenterol 1998;93:1583-5.
27. Rollhauser C, Fleischer DE, Nonvariceal upper gastrointestinal bleeding: An upadate. Endoscopy 1997;29:91-105.
28. Singh G, Ramey NSAID induced gastroitestinal complications. The ARAMIS Perspective - 1997. J Rhematol.
29. Bolten WW. Scientific rationale for specific inhibition of COX-2. J Rhematol 1998;51:2-7.
30. Yeomans N, Cook GA, Giraud AS. Selective COX-2 inhibitors: Are they safe for the stomach? Gastroenterology 1998;115:227-9.

31. Yeomans ND, Tulassay Z, Juha sz L, Ra'cz I, Howard JM, Rensburg CJV, Swannell AJ, Hawkey CJ. A comparison of omeprazole with ranitidine for ulcers associated with nonsteroidal antiinflammatory drugs. N Negl J Med 1998;338:719-26.
32. Hawkey CJ, Karrasch JA, Szczepan'ski L, Walker DG, Barkun A, Swannell AJ, Yeomans ND. Omeprazole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. N Engl J Med 1998;338:727-34.
33. Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, Winton TL, Rutlegde F, Todd TJR, Roy P, Lacroix J, Griffith L, Willian A. Risk factors for gastrointestinal bleeding in critically ill patients. N Engl J Med 1994;330:377-81.

SUBSCRIBE

Subscription Rates
(India) in Rupees

	1 yr.	3 yrs.
Personal Rate	400	1000
Standard Rate	500	1200
Reduced Rate	250	x
Life Membership	**3500**	**10 Yrs**

Standard rate is for Institutions and Libraries
Reduced rate is for undergraduate students, interns and those under-going post graduate courses
Foreign

	1 yr.	3 yrs.
Gulf Countries	100 SR	275 SR
Rest of the World	$US 100	$US 200

JK-PRACTITIONER The International Journal of Current Medical Science & Practice

Name ____________________

Address ____________________

____

Institution/Hospital ____________________

Please tick box

☐ Yes send me JK-Practitioner

☐ Personal ☐ Standard ☐ Reduced

☐ I enclose a cheque/bank draft payable to the editor, JK Practitioner at Srinagar. (SBI, JK Bank or Grindlays Bank).

Expiry date ____________________

Signature ____________________

Date ____________________

Please return this order form to Dr. G.M. Malik, P.O.Box 884 GPO
Srinagar 190 001 (Kashmir)

FLOW CYTOMETRY IN URO-ONCOLOGY

Chithrathara K, M.D.; Gangadharan V.P., D.M.; Subramaniam P, M.Ch.

Flow cytometry (FCM) allows a high speed analysis and sorting of cells according to morphological, molecular, biophysical and functional cellular features which can be correlated with each other in multi parameter computer assisted inst uments. Mono dispersion, quantitative cells staining and high resolution analysis are essential to all FCM analysis.

DNA FCM is independent of cell proliferative activity, however, the proportion of the cells in the S phase of the cell cycle increase with increasing DNA excess in many solid tumors.

Use of Flow Cytometry:

Assessment of DNA content within the cell, the parameters looked into are ploidy, number of aneuploid cell lines and DNA index (ratio of tumor cells to normal G1-G0 cell). It also gives an estimate of cell size, cytoplasmic granularity, cell viability, surface marker phenotype and enzyme content. With high resolution a numerical chromosomal aberration involving more than one chromosome should routinely be detectable.

Sample Preparation:

1. Desegregated cell or nuclei in suspension.
2. Nuclei extracted from tissue fixed and paraffin embedded by Hedley's technique[1].

Method of FCM:

The cells are stained with fluroescent dye that bind quantitatively to DNA. The stained cells are then analyzed in a flow cytometer which excites the dye with a laser beam and measure the fluorescence emitted by individual cell as they pass before a photo multiplier tube one at a time. The fluorescent data is compiled on a histogram indicating the distribution of DNA content. A straight forward method to qualify immunostained cells is to count the fluorescent cells above a threshold empirically determined on a control histogram representation. More reliable method of data analysis include Histogram Shape Dependent Method (HSD), subtraction of blank from rest histogram and Kolmogorov - Smirnov statistical test[2]. In the case of very low antigen expression, fluorescent microscopy remained the only valid method.

Limitation:

1. Cells must be in a single cell or nuclei suspension to be analyzed and so there can be loss of tissue morphology. However, suitable technique have been developed for most tumors, including preparation of nuclear suspension recovered from thick section.
2. Inflammatory cells can form a hyperdiploid cell fraction which makes interpretation of standard FCM difficult.
3. DNA content correlates with model chromosome content, no indication is given about which chromosome is involved. Even good histogram miss important lesions such as trnas location and deletion.
4. In low grade tumors, most cells are diploid, so it mostly gives false negative result.
5. Major drawback of FCM is its cost.

Major Application of FCM in Clinical Practice:

1. Diagnosis of Malignancy:

Demonsration of an aneuploid cell population suggest a diagnosis of malignancy when the morphological changes are equivocal. This is well applied in detection of residual tumor after primary cytotoxic therapy. In these cases, persistence of aneuploid cells would constitute the need for further adjuvant therapy. So also, DNA flow cytometry help to determine whether two anatomically separate tumors of similar histology (synchronous or metachronous) are independent or metastatic. A different DNA index after a long time distinguishes second cancer from a relapse.

It may soon provide finger print type information of an individual patient tumor. In difficult areas of cytology eg., bladder irrigates, effusion, sputum and bronchial washings DNA, FCM emerges as a

JK-Practitioner 1999; 6(4):259-264

From the Departments of Surgical Oncology (Chithrathara), **Medical Oncology** (Gangadharan) **Regional Cancer Centre Trivandrum and Department of Oncology** (Subramaniam) **Medical College Trivandrum, India**

Recieved September 1998 Accepted June 1999

Correspondence to : Dr. ChithratharaK. Chithira Left end Road Jai Nagar Trivandrum - 695 001, India

powerful diagnostic tool.

2. **Specific diagnosis:**
   Currently specific histological diagnosis can be made with some degree of certainty only in the lympho proliferative disorders.

3. **Prognosis:**
   High 'S' phase fraction and high DNA index values seemingly even interrelated, have emerged as adverse prognostic factor for survival in lung, breast, bladder, prostate and colon cancer.

4. **Treatment design:**
   As already mentioned, serial studies during a patient's disease may help to delineate residual disease and thereby, need for further therapy is determined. DNA FCM for assessment of cell cycle distinction can be coupled with cycle traverse rate and growth fraction and is useful for optimization of scheduling of drugs.
   FCM analysis of fluorescent drugs such as anthracy cline may gain importance as drug sensitivity test both in vitro and in vivo. DNA reactive drugs such as Cisplatin can alter the sensitivity of chromatin to denaturation which can be detected by FCM using acidine orange as a chromatin probe. FCM assay for hormone receptor analysis will help to maximize the anti tumor effect of hormonal or chemotherapy.
   Evaluation of blood lymphocyte subsets by FCM will be necessary to monitor the efficacy of biological response modifier aimed at restoring immuno deficiency or imbalance.

5. **Detection of cytokinetic markers:**
   The major cytokinetic determinants for tumor cell kill include growth fraction, cell cycle distribution and cycle traverse rate.
   Cell cycle stage distribution can be easily assessed by FCM analysis of DNA content and has the following applications:
   a. Characterisation of vrious cytokinetic properties of haematologic and solid tumors.
   b. Assessment of cell effect of various anti tumor agents.
   c. More rational design of various combination chemotherapy regimens.

6. **Use of monoclonal antibody in FCM:**
   Function assays of drug and radiation resistance are being developed in the laboratory and in the long run this may prove to be the most clinically useful function of FCM. Drug resistance can be due to various mechanisms:
   1. Drugs fail to get concentrated in the cell: mediated by over expression of any energy dependent transmembrane pump (P_{170} glyco protein Mdrl gene product).
   2. Damage to the target molecule (usually DNA) is prevented by a thiol dependent free radical scavenging system.
   3. Repair of the damage

   By using monoclonal antibody FCM can quantitate P glycoprotein and give a measure of the heterogeneity if its expression or detect small subgroup of antigen positive cells.

Urological cancers pose a unique challenge to the uro-oncologist since the social acceptance, family life and in general the quality of life is considerably influenced and dependent on the correct management. But at the same time cure should not be dispensed with. With innumerable uses of FCM theoretically, it is exprcted to have a definite role in the diagnosis, management and follow up of patients with urological malignancies. How far is this true? A discussion on the clinical usefullness of FCM with respect to each urological cancer follows.

Carcinoma Bladder:

Bladder is particularly amenable to examination with FCM since specimens can be easily collected. In 1980 Colleste et al[3], reported a serie of patients studied with FCM using bladder irrigation. Since then Transitional cell carcinoma (TCC) of the bladder has been the most extensively studied urologic tumor with FCM. The degree of ploidy is generally related to grade and stage of tumor, diploid tumors are of generally low grade and aneuploid tumor are of high grade.

DNA content is an independent predictor of survival, but only in PT Grade 3 tumor it enhances the prognostic information above the traditional stage grade[4]. Report on a multicentric prospective trial using DNA content and S phase fraction measured by FCM as predictors of survivals and recurrence showed that both are poor predictors of recurrence when measured on a single superficial bladder cancer[5]. But in general aneuploid tumors recur three times more frequently than diploid tumors. Furthermore, aneuploid was associated with higher stage, poorer grade, multifocality, Her—2/new and P 53 expression high S phase fraction (SPF) correlated with higher grade and stage.

DeVare White et.al[6] also had similar observation - all patients with aneuploid tumor had recurrence while only 29% of patients with diploid tumour recurred. Non - tetraploid aneuploid tumors were more aggressive. In

20 of 28 patients with recurrence, a change in ploidy from diploid to aneuploid was noted at the time of recurrence.

The number of proliferation and activation do not always measure the same parameters even in the same stage. FCM study[7] of the nuclear antigen Ki 67, membrane antigen T_{43} and epidermal growth factor receptor (EGFR) revealed a preferential expression of T_{43} in invasive bladder cancer. Ki 67's expression was independent of tumor stage and no tumour was found to strongly express two markers simultaneously. Expression of surface glycoprotein T_{138} antigen indicates bad prognosis and is complementary to FCM DNA ploidy in assessing prognosis. Among patients with diploid tumors, none (0/26) had cancer death if T_{138} antigen was not expressed and 33% had cancer death if T_{138} antigen was expressed. In aneuploid tumors, mortality was reported in 12/19 cases, if T_{138} was expressed and only in 2/10 cases death when T_{138} was not expressed[8]. Measurement of DNA and cytokeratin, and epithelial marker, improves the accuracy of prognostication of a given tumor.

Few analysis was focused upon DNA ploidy pattern following cystectomy. One such study is reported by Toyoto K[9], where he studied 478 paraffin embedded samples of 63 patients. He could find significantly good correlation among DNA ploidy pattern and intravesical involvement, but were not among the DNA ploidy and tumor stage and grade. In an analysis of the Feulgen stained paraffin sections, Fossa et al[10], found that patients with advanced diploid tumour (Stage II-IV) had better actuarial survival rates at 18 months, than those with non diploid tumors. But his survival advantage disappeared at 24 months, which reflect the slower growth rate of tumor already beyond surgical cure. However DNA ploidy did not add any prognostic information to that obtained from histopathologic examination.

DNA ploidy and proliferative index influence the incidence of metastasis. Metastasis was shown to be more frequent with aneuploid tumor (29% versus 8% in diploid tumors)[11]. The ploidy in the primary tumor and metastasis were reported to be non identical in 50% of cases.

Most of the cases of carcinoma in situ are aneuploid. The combination of more than one aneuploid cell line, a high proliferative index, high percentage S phase portended a particular 5 yr. survival in patients with diploid bladder tumor was 91% and in tetraploid tumor it was 83%[12].

Specimen Collection

Saline washing are more accurate since it yields more and better preserved cells[13]. First voided sample has to be avoided because of cell degeneration and thus misinterpretation. Confusing abnormalities can occur after radiotherapy, BCG instillation, intravesical chemotherapy and post contrast urine. Urinary tract infection (UTI) and calculi can also cause misdiagnosis.

Conventional Cytology and FCM

The sensitivity reported are 83% for FCM, 61% for cytologtic studies and 60% for 3 voided samples[14]. Giella et al[15] documented high specificity for cytologic studies (less false positivity). But they reiterate that false positive results with FCM DNA ploidy and cytologic studies were equally predictive of recurrent TCC progressively with time. But for any given examination FCM was more likely to detect and predict TCC recurrence and was more likely to predict natural history of the patients disease.

Comparison of FCM with other modalities of detection of DNA content

Image Analysis

Quantitative fluorescent imaging combines quantitatives biochemical analysis and more subjective evaluation of individual cell. A computer controlled mircroscope automatically scan the nucleus of cells in smear and quantitate the emitted fluorescence, which in turn reflects the nucleic acid content. Voided urine specimen can be used for this, since it can be interpreted even on few cells.

Multiparameter image analysis can also be performed. Labelled monoclonal antibodies to various tumor markers used in conjunction with DNA fluorescence can increase specificity of image analysis in bladder cancer detection. So also, this technique is more sensitive especially in detecting low grade bladder tumor than cytology and FCM.

Fluorescence in situ hybridisation (FISH):

FISH allows visualization and quantification of gene and chromosomes on a cell by cell level and can easily be applied to urinary cell. The frequency of FISH aberration in PTa was reported to be 47%, PTI - 85% and P_{T2-4}-98%. This shows grater difference between P_{T0} and P_{T1} and this argues against including both as superficial tumor[16]. FISH appeared to be more sensitive for detection of quantitative DNA aberration than FCM. This has placed FISH in second place, with regard to sensitivity preceded by image analysis and followed by FCM, while cytology and FISH have the highest specificity.

Prostate Cancer

FCM DNA ploidy analysis in carcinoma prostate faces several unique challenges. First of all this tumor has a protracted natural history, so it is difficult to interpret prospective trials. Eventhough there are reports using core biopsies and fine needle aspiration of DNA flow cytometry, radical prostectomy specimens are routinely used for DNA ploidy analysis, this might be due to the expected sampling error of a simple core biopsy and the low signal to noise ratio (ratio of tumor cells to normal cells). Further more, there may be great heterogeneity, so the polidy in one area differs from polidy in other areas.

Two types of heterogeneity are seen. In Type A, aneuploid pattern is seen in association with diploid pattern. In Type B heterogeneity, multiple aneuploid pattern with different DI values are seen. Poorly differentiated tumors showed heterogeneity more frequently (67%) than well differentiated tumors. Similarly stage I tumors had low heterogeneity (14%) when compared to 57% heterogeneity in stage D tumors[17].

FCM of chromosomal aberration, DNA ploidy and S phase fraction were studied on 57 men with prostate cancer by Bratt O et al[18]. He observed that among the above three variables, S phase fraction was the best predictor of survival. However, he could not answer whether SPF would add any prognostic information to tumor stage and grade.

Reports on two retrospective analysis on localised prostate cancer (B stage) were giving conflicting results. Montgomery et al[19] reported poor survival for patients with aneuploid tumors than for diploid or tetraploid tumors. He had followed up 2611 patients for 9 years. Ritchie et al[20] followed up 109 patients for 54 years and found no correlation between ploidy and survival. According to Himd, only the grade of tumor influences the survival Another study by Ring et al[21] also was in agreement with Richie et al[20] but after critically analysing he concluded that aneuploid tumours not treated with radical surgery or those with positive margin do appear to be at a disdavantage.

Pindur A[22] and Tinari N et al[23] detected a good correlation of DNA ploidy with other pathological parameters like grade, size, extra capsular extension and positive surgical margin. Furthermore Tinari et al pointed out that survival correlation was better in locally advanced or metastatic prostate cancer that T1/T2 tumors.

"Ploidy does not predict length of survival once prostate cancer becomes disseminated." This contradicting statement to Tinari N et al came from Deitch A A and DeVere White R W[24]. However they found ploidy abnormalities useful to diagnose persistent tumor after radiotherrapy.

Prognosis in locally advanced prostate cancer (Stage C) also is influenced by DNA ploidy. In stage C, 46.7% of tumor were found to be aneuploid and the recurrence rate of aneuploid tumor was 63.6% whereas for tetraploid tumor it was 50%[25]. But the 10 year survival rate of aneuploid stage C patients was 64%. So it is prudent not to alter treatment decision, based on DNA ploidy alone.

Lieber M M[2] in the Mayo clinic routinely used ploidy information decide on adjuvant therapy after radical prostatectomy.

Statistically significant difference in recurrence was noted between aneuploid and diploid tumors in metastatic prostate cancer. Reports shows that aneuploidy with multiple stem lines has worst prognosis[27] and diploid tumors have best prognosis with the non tetraploid aneuploid and tetraploid tumor coming midway between.

Renal Cell Carcinoma

The most critical determinant of prognosis in renal cell carcinoma (RCC) is the stage at diagnosis[28,29]. Most studies about DNA ploidy in RCC showed that it correlated well with survival.

124 patients were followed up to 9 years by Eskelinen and co-workers[30] to study the survival and DNA ploidy. DNA ploidy was an independent prognostic factor in recurrence free survival and survival of M_0 tumors. Surprisingly they observed that DNA aneuploidy was related to favourable response in both multivariate and univariate analysis. They attribute this to better response of these tumours to treatment.

In vivo incorporation of iodoxy uridine and its analysis by antibodies using FCM[31], the mean potential tumor doubling time was found to be 20.3 days compared to 137.7 days of normal cortical tissue. In diploid tumors, the doubling time was 37.4 where as in aneuploid it was 12.5 days and this in turn has got an impact on survival outcome. Tumor hetergeneity in RCC is 45% which increases with grade of tumor[32].

TCCF of renal pelvis and ureters

The prognostic implication of DNA ploidy are same as that of bladder TCC and was shown to correlate with histologic findings. Oldbring and associates[33] found that all grade III and 50% of grade II tumors are aneuploid. High grade cells on FCM or image analysis in the absence of a low grade superficial bladder tumor warrants the search for malignancy in renal pelvis or ureters or prostatic urethra[34]

Testicular Neoplasm

In carcinoma-in-situ (CIS), the DNA FCM is complimentary to histology. In a study by Hittmair A[35], in all but one case, the DNA indices of CIS and invasive tumors were identical. So DNA FCM is helpful in follow up of patient who stand high risk for development of CIS. 50% of men with CIS was found to have aneuploid in the semen compared to 0% in normal men[36]. But the possibility of inter testicular compression by mass of semen passage makes DNA ploidy unreliable in screening of testicular compression by mass of semen passage makes DNA ploidy unreliable in screening of testicular cancer patients.

30-40% of clinical stage I Non seminomatous Germ Cell tumor (NSGCT) has got occult retroperitoneal metastasis which is undetectable by the available non-invasive staging methods[37]. Eventhough almost all of NSGCT are said to be aneuploid, the FCM detection of aneuploid cells in the G_2M and 'S' phase correlated with lymph node metastasis. Concordant results are observed in 76.5% cases after retropentoxed lymph node dissection. FCM is also used to predict recovery of sperm cell production after treatment. A low pretreatment percentage of condensed haploid cells was correlated with lack of one year recovery[18]. Most of malignant Leydig cell tumor are aneuploid, so aids in diagnosis.

Adernal Tumor

The distinction between benign and malignant adrenal tumor is difficult and many pathologist rely on venous and capsular invasion to call a tumor malignant or rely on metastasis to label it malignant. Klien et al[39] showed that aneuploid was present only with malignant adrenal tumor and so has got a major role to play in their diagnosis. But Rain Water et al[40] disagrees with the above observation, since his three patients with benign adrenal neoplasm also had abnormal DNA.

Conclusion

Rapid technological advance had lifted FCM to one among the essential diagnostic armamentarium in oncology. Its pivotal role in the field of lymphoreticular malignancy is well recognised.

FCM analysis of DNA and its role in the diagnosis and management of urological cancer is less well defined. Cacinoma-in-situ of urothelium is one area where FCM DNA ploidy sensitivity is high. This helps to select patients for random biopsies and if negative keep renal pelvis, ureter and prostatic urethra under scrutiny.

Detecting residual tumor in bladder cancer, prostate and germ cell tumor will be of great clinical utility. However in tumors like renal cell carcinoma the detection of neither high risk patient nor residual cancer may not be of much help since there is no effective adjuvant therapy.

In majority of studies FCM, DNA parameters well correlate with recurrence and survival, and are complementary to grade and stage in assessing prognosis. But translating this to treatment, how far are we going to be successful? The era of detection of cancer at chromosomal level and gene therapy open new horizon for FCM and could answer the above question.

References:

1. Hedley D W., Fried Lander ML., Taylor I W., et al: Method for analysis of cellular DNA content in paraffin embedded pathological material using flow cytometry. J Histochem cytochem 1983;31:1333.
2. Chabanas A., Rambeaud J J., Huo H H., Seigneurin D., Lawrence J J., Limits of flow-cytometry histogram analysis methods to assess bladder tumor antigen expression. Analytical cellular pathology. 1997;13(1):39-47.
3. Collste L., Darzynkiewicz Z., Tranganos F., et al: Flow cytometry in bladder cancer detection and evaluation using acridine orange metachromatic nucleic acid staining or irrigation cytology speeimens J. Urol. 1980;23:478-485.
4. Bittard H., Lamy B., Billery C.: Clinical evaluation of cell deoxyribonucleic acid content measured by flow cytometry in bladder cancer. J. Urol. 1996 Jun; 155(6):1887-91.
5. Tetu B., Allard P., Fradet Y., Roberge N., Bernard P.: Prognostic Significance of Nuclear DNA content and S-phase fraction by flow cytometry in primary papillary superficial blader cancer. Human pathology 1996 Sep.; 27(9):922-26.
6. DeVere White R.W., Deitch A.D. West B., et al.: The predictive value of low cytometric information the clinical management of stage 0 (Ta) bladder cancer. J. Urol. 1988;139:279-282.
7. Lacombe L., Gauthier J., Lafleur L., Fradet Y.: Clincial value of the study of proliferation and cell activation antigens with flow cytometry in bladder cancer. Progres en Urologie 1996 Dec.; 6(6):907-12.
8. Fradet Y., Tardif M., Bourget L., et al. Clincial cancer progression in urinary bladder tumors evaluated by multiparameter flow cytometry with monocolonal antibodies. Cancer. Res. 1990;50: 432-437.
9. Toyota K.: Studies on nuclear DNA in bladder cancer using flow cytometry. Hokkaido J. Med. Sci. 1996;Jan; 71(1):45-53.
10. Fossa S.D., Kaalhus O., Scott Knudsen O.: The clinical and histopathological significance of Feulgen DNA values in transitional cell carcinoma of the human urinary bladder. Eur. J. Cancer 1977;13:1155-1162.
11. Tribukait B.: Flow cytometry in assessing the clinical aggressiveness of genitourinary neoplasms. World J Urol. 1987;5: 108-122.
12. Whang I.S., Benson M.C.: Flow cytometry in urologic practice. Advances in Urology 1992; Vol.5 p11-32.
13. Trott P.A., Edward L: Comparison of bladder washings and urine cytology in the diagnosis of bladder cancer. J Uro. 1973;110:664.
14. Badalament R.A., Hermansen D.K., Kimmel M., et al.: The sensitivity of bladder wash flow cytometry, bladder was cytology and voided cytology in the detection of bladder carcinoma. Cancer 1987;48:109-118.

15. Giella J.G., Ring K.S., Olsson C.A., et al.: The predictive value of flow cytometry and urinary cytology in the follow-up of patients with transitional cell carcinoma of the bladder. J. Urol. 1992 Aug; 148(2pt,1): 293-296.
16. Sauter G., Gasser T.C., Moch H., Richter J., Jaing F., Albrecht R., Novonty H., Wanger U., BubendrofL., Mihatsch M.J: DNA aberrations in urinary bladder cancer detected by flow cytometry and FISH. Urological Research. 25 Suppl. 1997;1:837-843.
17. Michinga S., Ariyoshi A., Kinjo M., Sagiyama K.: Flow cytometry analysis of the DNA content of the prostate cancer-study on the tumor heterogeneity in the prostate cancer: Japanese J. Urol 1996 Jun;87(6): 937-41.
18. Bratt O., Andreson H., Bak-Jensen E., Baldetorp B., Lundgren R.: Metaphase Cytogenetics and DNA flow cytometry with analysis of S-phase Fraction in prostate cancer: influence on prognosis. Urology. 1996 Feb.;47(2):218-24.
19. Montogomery B.T., Nativ O., Blute M.L., et al.: Stage b prostate adenocarcinoma. Arch. Surg. 1990;125:327-331.
20. Ritchie A. W.S., Layfield L. I., Hannah J., et al.: Relationship of DNA content to conventional prognostic facors in clinically locazied carcinoma of the prostate. Br. J Urol. 1988;62:254-260.
21. Ring K.S., Karp F.S., Olsson C.A., et al.: Flow cytometric analysis of localized adenocarcinoma of the prostate. The use of archival DNA analysis in conjunction with pathological grading to predict clinical outcome following radical retropubic prostatectomy. Prostate 1990;17:155-164.
22. Pindur A., Chakraborty S., Velchy D.G., Wheeler T.M.: DNA ploidy measurements in prostate cancer: difference between analysis and flow cyutometry and clinical implication. Prostate. 1994 Oct;25(4):189-98.
23. Tinari N., Natoli C., Angelucci D., Tenaglia R., Fiorentino B., Di Stefano P., Amatettic C., Zezza A., Nicolai M., Iacobelli S.,: DNA and S-phase fraction analysis by flow cytometry in prostate cancer. Cancer 1993 Feb.;71(4):1289-96.
24. Deitch A.D., DeVere White R.W.: Flow cytometry as a prdictive modal;ity in prostate cancer. Human Pathology. 1992 Apr.;23(4): 352-9.
25. Nativ O, Winkler H.Z., Raz Y., et al.: Stage C prostatic adenocarcinoma: Flow cytometric nuclear DNA ploidy analysis. Maya Clin Proc 1989;64:911-919.
26. Lieber M.M.: Prognostic impoirtance of nuclear DNA content measured by flow cytometry for patients with adenocarcinoma of the prostate. Urologia Internationals 47 Supl. 1991;1:74-6.
27. Trivukait B.: Flow cytometry in surgical pathology and cytology of tumors of the genito-urinary tract, in Koss L G, Coleman D V (eds;) Adv. Clin. Cyto. 1984;2:163.
28. Grignon D.J., Ayala A., El-Naggar A., et al: Renal cell carcinoma. Cancer 1989;64:2133-2140.
29. Chin J., Pontes J., Frankfurt O.: Flow cytometric deoxyribonucleic acid analysis of primary and metastatic human renal cell carcinoma. J Urol. 1985;133:582—585.
30. Eskelinen M., Larsson P., Nordiling S.: prognostic evaluation of DNA flow cytometry and histo-morphological criteria in renal cell carcinoma. Anticancer Research. 1995 Sep-Oct.;15(58):2279-83.
31. Liungberg B., Larsson P., Roos G, Stenling R., Wilson G.: Cell kinetics of renal cell carcinoma studied with in vivo iododeoxyuridine incorporation and flow cytometry. J. Urol. 1993 Jun.; 151(6): 1509-13.
32. Kushima M., Konishi T., Okada Y., Tomoyoshi T., Kushima R., Hattori T.: Tumor heterogeneity in DNA ploidy of renal cell carcinomas as revealed by static cytofluorometry and flow cytometry. Japanese J. Urol. 1994 Mar.; 85(30): 473-80.
33. Oldbring J., Glifberg I., Mikulowski P., et al.: carcinoma of the renal pelvis and uretes following bladder carcinoma, Freqneucy, risk factors and clinicopathologic findings. J. Urol. 1989;141:1311.
34. Walsh P.C., Retik A.B., V Aughon Jr. E.D. Wein H.J.: Cambell's Urology 7th edition, WB saunder. 1998;p. 2353.
35. Hittmair A., Rogatsch H., Feichtinger H., Hobisch A., G.: Carcinoma in situ of the testis detected by DNA flow cytometry of testicular fine - needle aspirates. Cytometry. 1994 Dec.;17(4): 327-31.
36. Giwercman A., Clausen O.P. Skakkeback N.E.: Carcinoma in situ of the testis. Aneulploid cells in semen. Br. Med. J. 1988;296: 176201764.
37. De Riese W., Walker. E.B., de Riese C., Ulbhright T.M., Crabtree W.N., Messemer J., Jones J.A, Hinkel A., foster R.S., donohue J.P.: quantitative DNA measurement by flow cytometry and image analysis of human nonseminomatous germ cell testicular tumors. Urological Research. 1994;22(4): 213-20.
38. Fossa S.D., Melvik J.E., Juul N.O., Pettersen E.O., Amellem O., theodorsen L.: DNA flow cytometry in sperm cells from testicular cancer patients. Impact of different treatment modalities on spermatogenesis. European Urology 1991;19(2):125-31.
39. Klein F.A., Kay S., Ratliff J., et al.: Flow cytometric determinations of ploidy and profliferation patterns of adrenal neoplasms: An adjunct to histological classification. J.Urol. 1985;134:862-866.
40. Rainwater L. M, Young W., Farrow G., et al.: Flow cytometric analysis of deoxyribonuclic acid ploidy in benign and malignant aldosterone-producing neoplasms of the adrenal gland. Srug. Gynecol. 1989;168:491-496.

MULTIPLE MYELOMA - STATUS OF HIGH DOSE THERAPY WITH STEM CELL TRANSPLANTATION

Gangadharan V.P. M.D., D.M.

Introduction

Multiple Myeloma is a hematologic malignancy, characterised by clonal proliferation of plasma cells. It is predominantly a disease of the elderly age groups. Patients usually present with symptoms related to anemia, bone disease characterised by lytic lesions and pathologic fractures, renal failure due to hypercalcemia and/or massive Bence-Jones proteinuria, and recurrent infections due to immunosuppression. Median survival is 30-36 months, approximately 50% achieving a remission by conventional treatment with Melphalan and Prednisolone. Survival is still worse in high risk patients with large tumor burden and median survival of 9-12 months is reported with the addition of other alkylating agents and Doxorubicin to this regimen[3,4,5]. High dose glucocorticoids especially when combined with continuous infusions of Vincristine and Doxorubcin (VAD) show ill sustained responses in alkylating agent resistant myeloma[6,7]. Interferon appears maximally active in patients with low tumor load following an effective induction treatment[8].

High Dose Therapy (HDT)

Myeloablative treatment with high dose chemotherapy. (HDCT)± Total Body Irradiation (TBI) has been evaluated for the treatment of myeloma for the last 10 years with promising results in terms of responses and durable remissions even in refractory myelomas[9,10]. Though higher responses were noted, complications of myelosuppression were common. Myelosuppression has been overcome with the use of autologous, syngenic or allogenic haematopoietic support[11]. Sources of heamatopoietic stem cells were:

1. Autologous bone marrow (unpurged / purged)
2. Peripheral blood stem cells
3. Marrow + blood stem cells
4. CD34 + progenitor cells
5. Allogenic Bone marrow.

The trials were encouraging and promising for high dose therapy with autologous transplantation as an effective salvage therapy. Chemosensitive relapses and primary refractory patients fared well for this regimen[12,13] and refractory relapses showed a poor outcome[14], with a median remission duration of 5 months.

Complete remission after bone marrow transplantation is defined[15] as the following.

1. absence of detectable monoclonal immunoglobulin in serum and detectable free light chains in urine on either conventional immunoelectrophoresis or immuno fixation.
2. absence of apparent multiple myeloma cells in the marrow on conventional cytologic analysis.

Disappearance of bone disease has not been recorded as a criteria for complete remission.

A variety of HDCT regimens with or without varying TBI regimens have been used in HDT in myeloma with conflicting reports. EBMT has published results in 384 patients who underwent either autologous bone marrow transplantation or peripheral blood stem cell transplantation[16]. A great variety of conditioning regimens have been used. In a multivariate analysis of prognostic factors for survival or progression free survival, inclusion of melphalan and non-TBI conditioning regimens appeared favourable, though the optional conditioning non-TBI regimen in terms of the drugs dose and scheduling cannot be clearly defined.

Although selection bias cannot be excluded in this non randomized trial, the report by Goldschmidt[17] et al favour the use of melphalan alone over TBI containing regimens in the high dose treatment regimens of multiple myeloma. The lack of advantages wih the TBI containing regimen with comparatively higher toxicity corroborates with the EBMT results.

Eversince the early reports of McElwain[9] et al with 140mg/m^2 of Melphalan, several dose escalations have been attempted aiming at better results. Barlogie[18] et al showed in dose escalation studies that 140mg/m^2 of

JK-Practitioner 1999; 6(4):265-269

From the Department of Medical Oncology (Gangadharan)
Received October 1998 Accepted June 1999

Correspondence to : Gangadharan V.P., Head, Division of Medical Oncology, Regional Cancer Centre, Thiruvananthapuram.

Melphalan is the optimal dosage, since $200mg/m^2$ induced more toxicity without a higher remission rate.

Very few studies have attempted to delineate prognostic factors of importance in the outcome of patients treated with high dose chemotherapy followed by autologous[19] or allogenic bone marrow transplantation[20]. In the European study[21], the following factors were predicitive for longer survival and freedom from progression, in a univariate analysis. In an autologous set up. Male sex, age less the 45 years, low serum B_2 microglobulin value at diagnosis, prior administration of only one treatment regimen, response on conventional chemotherapy immediately pre transplant and the use of a preparatory regimen including melphalan. Stage 1 disease at diagnosis, male sex, responsive disease immediately pretransplant and use of preparatory regimen including melphalan were independent predictive variables for longer survival, in multivariate analysis. Progression free survival was significantly better for patients who were in complete remission after transplantation, as compared to those with persisting sign of disease.

In multivariate analysis of the EBMT trial, favourable pre autotransplant prognostic factors were low B_2 microglobulin (<4mg/l) at diagnosis, response to the conventional treatment either by complete or partial remission and one line of previous treatment regimen[16]. Other factors that seem to be of importance in survival following auto transplants are the serum creatinine value, the albumin level and the chromosome pattern. Abnormalities on chromosome 11 combined with deletions of chromosome 13 or any translocation appear to have negative prognostic impact for survival[22].

Favourable pretransplant prognostic factors for survival in allogenic bone marrow transplant were female sex, stage 1 disease at diagnosis, one line of previous treatment, complete remission, IgA myeloma and low B_2 microglobulin level (<4mg/l)[15]. Most important post transplant prognostic factor was to enter a complete remission. Grade III to IV Graft Versus Host disease (GVHD) was associated with poor survival.

High dose chemotherapy as unfront treatment with autologous transplantation.

The encouraging response of HDT as salvage therapy led to the use of HDCT with autologous transplantation in untreated myelomas. Response rate varied from 70-90% with a median survival of 4-5 years[23] and complete remissions upto 75% has been reported[24]. 1FM 90 trial[25], a randomized trial, compared conventional chemotherapy with high dose chemotherapy. High dose therapy significantly improved both the EFS and OS and recommended this especially in the management of younger patients.

Survival		CC	HDT
Median	EFS	18/12	27/12
	OS	37.4/12	Not reached
Projected 5 yr	EFS	10%	28%
	OS	12%	52%

EFS - event free survival, OS - overall survial.

CC = conventional chemotherapy, HDT = High dose therapy: Similar conclusions were reached by S.W.O.G[26] also.

Fermand[27] et al explored the possibility whether high dose therapy with autologous blood stem cell transplantation (ABSCT) at the time of disease progression following conventional chemotherapy (VMCP) can have the same results like IFM 90 trial. Overall survival rates at 3 years were 74.5% and 73.5% in the V.M.C.P and HDT groups respeotively, (SD5%) and suggested that HDT with ABSCT as front line dose not confer a survival advnatage over conventional therapy with early resuce by HDT in young aggressive myelomas. In order to make the remissions more durable, intensive treatment is combined with maintenance therapy with alfa interferon in different trials[28,29]. Patients who achieved complete remission following high dose therapy showed a statistically significant prolongation of remission with alfa interferon therapy and 49% remained in remission four years after high dose treatment. Other stratagies for control of minimal residual disease, following high dose therapy, like maintainance chemotherapy, Interleukin 2, Interleukin-4, Retinoids, B cell directed immunotoxin, Idiotype vaccination etc. are still in infancy.

Double transplants with repeated cycles of intensive therapy with autologous transplant has been attempted which could increase the chance for complete remission. Programmes using two sequences of transplantation have been tried with this aim[30,31]. The impact of such therapy on overall survival warrants further evaluation.

Allogenic transplantation for multiple myeloma

Allogenic transplants for multiple myeloma have been associated with significant acute toxicity[15,32], probably because they were all previously heavily treated and with advanced disease. Allogenic transplants are limited to a few patients due to the need for HLA matched donors. Further, the outcome is poor in elderly patients aged more than 55 years. The probability of long term disease control is high with allogenic transplants, since the grafts are free of tumor cells. Graft vers myeloma effect akin to the graft vers leukemia effect in leukemia may also play a great role in the control of the disease[33,34,35].

Till now, over 500 allogneic transplants have been performed worlwide for multiple myeloma. Majority of them had TBI and chemotherapy as conditioning regimen. The largest reported series is the 162 patients from EBMT registry. Overall, published results indicated that 33% to 58% of all patients receiving HLA matched allografts achieve a complete remission, with 30-50% of the CR remaining disease free 3-6 years after transplantation[15,36,37,38,39]. Transplant related mortality was as high as 56%[31]. Less intensive optimal conditioning regimens, T cell depleted marrow combined with graded return of specific T cell subsets, allogenic peripheral blood stem cell transplantation or the higher doses o CD34+ selected cells[40] may all help in bringing down the mortality by reducing the toxicity and facilitating an early engraftment.

Auto vrses Allo Transplants in Myeloma.

Auto transplants are available to more patients than transplants Allo, HLA matched donor non availability bringing down the rate of allo transplants. GVHD and other acute toxicites are less in auto transplants and can be applied to a wider age range. The following conclusions were drawn from a case matched study of patients in the EBMT registry[41]. The median over all survival was significantly better with autologous transplantation than allogenic. CR was 48% in the allo group compared to 40% in the autogroup and the survival of these groups did not differ significantly. The higher transplant related mortality was conspicuous in the allogenic group. This resulted in a poor 4 year survival rate, although the relapse rates are lower in the allogenic transplant. Hence until the transplant related mortality is reduced, autologous transplants remain the treatment of choice.

PBSCT Versus ABMT for Autografting in myeloma.

Peripheral blood stem cell transplantation (PBSCT) is associated with rapid hematologic recovery than ABMT, after high dose chemotherapy for solid tumors or lymphomas[42,43,44] PBSCT has the potential advantage of rapid engraftment, less morbidity and cost benefit to replace ABMT in myeloma[29,45]. Use of hematopoietic growth factors for mobilising PBSC could increase the risk of collecting clonal myeloma cells along with stem cells[46m47] hence there is a theoretical risk of early relapse and decreased efficacy following the reinfusion of these tumor cells. Residual myeloma cells have been demonstrated in marrow harvests also and data suggest that PBSCT harvests may have a lower rate of contamination[48].

A comparison of ABMT versus PBSCT in previously untreated myeloma patients showed a faster engraftment and a shorter hospital stay in the PBSCT group; the survival outcome and the probability of relapse was the same for both groups[49]. Platelet recovery was significantly faster in the PBSCT Patients (19 Vs 33 days) than the neutrophil recovery (19 Vs 22 days). French group[50] reported a comparison of ABMT and PBSCT based on a retrospective analysis of 132 autologous stem cell transplant performed after first remission induction treatment in 18 French centres for multiple myeloma. The only significant benefit for PBSCT over ABMT was reduced time to neutrophil recovery. (13 days Vs 20 days, P value <0.001). There was no significant difference between the two groups regarding over all response rate, CR, RFS, OS and time to treatment failure. The delay in the neutrophil recovery in the British study in comparison with the French study, may be attributed to the difference in the mobilisation techniques.

Cost analysis showed that total cost was decreased by 17% in adults and 29% in children, with PBSCT than ABMT[43,44]. Global costs are lower and cost effective ratios are better with PBSCT, which may prove true in multiple myeloma also.

Future Trends

Molecular studies have not yet demonstrated cure in multiple myeloma irrespective of conventional chemotherapy, HDT with autologous transplantation or in most patients who undergo allogenic transplantation. Transplant related mortality can be decreased in an allogenic set up, with T cell purging and reducing the dose intensity of conditioning regimen. This may increase the chance of relapse. The theory of graft versus myeloma effect opens up a channel to explore the possibility of decreasing these relapses with later reinfusion of T cells or selected CD 34+ cells or other subsets of lymphocytes[45,46].

Post transplant interferon and idiotype vaccination has shown goood promise. Gene transfer to enhance immunogenesity, perhaps combined with some kind of so called suicidal therapy[51] may be an option - myeloma cells transduced by herpes simplex virus thymidine kinase gene as well as adjacent non transduced cells (by stander) and distant (distant by stander) non transduced cells may be killed when exposed to Gancyelovir. Newer studies are underway aiming at eradicating this deadly disease.

References:

1. Jagannath. S, Barlogie. B. Autologous Bone marrow transplantation for multiple myeloma. Hematol oncol clin. N Am; 1992;6:437-449.
2. Bergsagel DE, Sprague CC, Austin C, Griffith. K.M. Evaluation of new chemotherapeutic agents in the treatment o multiple myeloma. IV: L-phenyl alanine mustard. Cancer chemother rep., 1962;21:87-99.
3. Boccadoro. M, Marmont F, tribalto M, Avvisati. G, Andriani. A, Barbui. T, Cantonetti. M, Carotenuto. M, Comotti. B, Dammacco. f, Frieri. r, Gallamini. A, Gallone. G, Giovangrossi. P. Grignani. F, Lauta. V.M. Liberati. M, Musto. P, Neretto G, Petrucci. M.T., Resegotti. L, pileri. A and Mandelli. F. Multiple myeloma: alternating combination chemotherapy (VMCP/VBAP) is not superior to melphalan and Prednisolone (MP) keven in high risk patients. J Clin oncol., 1991; 9(3): 444-448.
4. Durie BGN, Stock-Novack. D, Salmon SE, Finley. P, Beckord. J, Crowley. J and Coltman. C.A. prognostic valve of pretreatment serrum B_2 micro-globulin in myeloma: a south west oncology group study. Blood; 1990;75:823-830.
5. MRC's working party on Leukemia in adults, prognostic features on the third MRC myelomatosis trial. Br J cancer 1980;42:831-840.
6. Barlogie. B, Smith. L, Alexanian R. Effective treatment of advanced multiple myeloma refractory to alkylating agents. New Engl J Med 1984; 310:1353-1356.
7. Alexanian. R, Barlogie. B, Dixon. D. High dose Gluco corticoid treatment for resistant multiple myeloma. Ann intern Med, 1986; 105:8-11.
8. Mandelli. F, Avvisati. G, Amadori. S, Boccadoro. M, Gernone.A, Lauta. VM, Marmont. F, Petrucci MT, Tribalto. M, Vegna. M.L, Dammaccoo. F and Pileri A. Maintainance treatment with recombinant interferon alfa-2b in patients with multiple myeloma responding to conventional induction chemotherapy. New Engl. J Med, 1990;322:1430-1434.
9. McElwain. T.J., Powles. R.L., High dose intravenous melphalan for plasma cell leukemia and myeloma. Lancet 1983;2:822-824.
10. Cunningham. D, Paz-Ares.L, Gore ME. High dose melphalan for multiple myeloma: long term follow up data. J. clin oncol 1994;12:764-768.
11. Barlogie. B, Gahrton. G, Bone marrow Transplantation in multiple myeloma. Bone marrow transplant 1991;7:71079.
12. Attal. M, Harousseau. J.L, Stoppa. A.M., Sotto. J.J, Fuzibet. J.G, Rossi. J.F, Casassus. P, Maisonneuve. H, Facon. T, Ifrah. N, Payen. C and Bataille. R. A prospective randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. N Engl. J. Med. 1996;335:91-97.
13. Attal M, Harousseau JL, Autologous transplantation in multiple myeloma. Gahrton G, Dune BGM (eds) Multiple myeloma. London, Arnold, 1996; p182.
14. Alexanian R, Dimopoulous M, Smith T: Limited value of myelo ablative therapy for late myeloma. Blood 1994; 83:572.
15. Gahrton G, Tura S, Ljungman P, Blade J, Brandt L, Cavo M, Facon T, Gratwohi A, Hagnbeek A, Jacobs P, Leurenzi AD, Lint MV, Michallet M, Nikoshelainen J, Reiffers J, Samson D, Verdonck L, Witte TD and Violin L. Prognostic factors in allogneic bone marrow transplantation for multi9p;e myeloma. J. Clin. Oncol 1995;13:1312-1322.
16. Bjorkstrand B, Ljungman P, Bird JM Samson D and Gahrton G: for the European group for bone marrow transplantation. Autologous stem cell transplantation in multiple myeloma. Results of the European group for Bone marrow transplantation. Stem cells; 13(Suppl.2) 140-6; 1995.
17. Goldschmidt H, Hegenbart G, Wallmeier M, Hohaus S, Engenhart R, Wannenmacher M and Haas R. High dose therapy with peripheral blood progenitor cell transplantation in multiple myeloma. Ann oncol 1997;8(3):243-246.
18. Barlogie B, Hall R, Zander A, Dicke K and Alexanian R. High dose melphalan with autologus bone marrow transplantation for multiple myeloma. Blood 1986;67:1298-1301.
19. Jagannath S, Barlogie B, Dicke K, Alexanian R, Zagars G, Cheson B, Lemaistre FC, Smallwood L, Pruitt K and Dixon DO. ASutologous bone marrow transplantaton in multiple myeloma. Identification of prognostic factors. Blood 1990; 76:1860-1866.
20. Gahrton G, Tura S, Ljungman P, Belanger C, Brandt. L, Cavo M, Facon T, Granena A, Gore M, Gratwohl A, Lowenberg B, Nikoskelainen J, Reiffers JJ, Samson D, Verdonck L and Violin L. Allogenic Bone marrow transplantation in multiple myeloma. N Engl J MEd 1991; 325:1267-1273.
21. Bjorkstrand B, Goldstone AH, Ljungman, Brandt L, Brunet S, Carison K, Prentice HG, Cavo. M, Samson D, Laurenzi AD, Verdonck LF, Proctor S, Ferrant A, Sierra J, Auzanneau G, Troussard X, Gravett P, Remes. K and Gahrton G. Prognostic factors in autologous stem cell transplantation for multiple myeloma. An EBMT registry study. Leuk Lymphoma, 1994;15:265-272.
22. Tricot G, Barlogie B, Jagnnath S, Desikan KR, Siegal D, Bracy D, Mattox S, Naucke. S, Munshi N and Sawyer J. translocations and 11/13 abonrmalities have a dominant prognostic implication and predict poor outcome in patients with multiple myeloma treated with high dose therapy and autotransplants, Blood 1996; 88(Suppl.1): 388A (Abstr. 1538).
23. Harousseau JL, Attal M, Divine M, Marit G, Lablond V, Stoppa A, Bourhis J, Cailot D, Boassan M, Abgrall J, Facon t, Linassier C, Cahn Y, Lamy T, Troussard X, createcos N, Pignon B, Auzanneau G, fand Bataille R. Autologous stem cell transplantation after first remision induction treatment in multiple myeloma. A report of the French registry on autologous transplantation in multiple myeloma. Blood 1995;85:3977-3985.
24. Cunningham D, Paz-Ares L, Milan S, High dose melphalan and autologous bone marrow transplantation as consolidation in previously untreated myeloma. J Clin oncol; 1994;12:759-763.
25. Attal M, Haroussoau JL, Stoppa AM: A prospective, randomized trial on autologous Bone marrow transplantation and chemotherapy in multiple myeloma. N. Engl J Med 1996;335:91-97.
26. Barlogie B, Crowlely J, Jagannath S, vesole D, Tricot G, Jacobson J and Salmon S. Superior outcome after early auto transplantation with 'Total therapy' compared to standard SWOG treatment for multiple myeloma (abstract). Blood 1995;86:207a.
27. Fermand JP, Ravaud P, Chevret S, Divine M. Lablond V, Belanger C, Dreyfus F, Troussard X, Brechignac C, Mariette X and Brouet I.C. High dose therapy and autologous blood stem cell transplantation versus conventional chemotherapy with high dose therapy rescue in multiple myeoma. Results of

a prospective randomised trial (abstract). Blood 1995;8:205a.

28. Attal M, Huguet F, Schlaifer D, Payan C, Lassoued S, Laroche M, Rosi JF, Fournie B, mazieres B, Pris J and Laurent G. Maintainance treatment with recombinant alpha interferon after autologous bone marrow transplantation for aggressive myeloma in first remission after conventional induction chemotherapy. Bone marrow transplant 1991;8:125-128.
29. Powles R, Raje N, cunningham D, Malpas J, Milan S, Horton C, Mehta J, Singhal S, Viner C, Treleaven J: Maintainance therapy for remission in myeloma with Intron-A following high dose melphalan and either an autologous bone marrow transplantation or peripheral stem cell rescue: Stem cells: 1995;13 sup;.2: 114-117.
30. Harousseau JL, Milpied N, laporte JP, Facon T, Tigaud JD, Casassus P, Guilhot F, Ifrah N and Gandhour C. Double intensive therapy in high risk multiple myeloma. Blood 1992;79:2827-33.
31. Jagannath S, tricot G, Vesole D, Desikan KR, Munshi N, Siegel D, Crowley J, Bracy D, Mattox S, Naucke S and barlogie B. total therapy with multiple myeloma. Blood 1996; 88(suppl. 1): 685 a (Abstr 2728).
32. Gahrton G, Tura S, Ljungman P, Belanger C, Brandt L, Cavo. M, Facon T, Granena A, Gore. M, Gratwohl A, Lowenberg B, Nikoskelainen J, Reiffers JJ. Samson d, Verdonck L and Violin L. Allogenic Bone Marrow transplantation in multiple myeloma. New engl J Med: 1991;325:1267-1273.
33. Aschan J, Lonnqvist B, Ringden O, Kumlien G and gahrton G. Graft versus myeloma effect. Lancet 1996;348:346.
34. Tricot G. Vesole DH, Jagannath S, Hilton J, Munshi N and Barilogie B. Graft-verrsus-myeloma effect: Proof of Principle. Blood 1996;87:1196-1198.
35. Verdonck LF, Lokhorst HM, Dekker AW, Nieuwenhuis HK and Petersen EJ. Graft versus myeloma effect in two cases. Lancet 1996;347:800-801.
36. Bensinger WI, Buckner CD, Anasetti C, Clift R, Storb R, Barnett T, Chauncey T, Shulman H and Appelbaum FR: Allogenic marrow transplantation for multiple myeloma. An analysis of risk factors on outcome. Blood 1996;88:2787-2793.
37. Seiden MV, Schlossman R, Anderson J, Freeman A, Robertson M, Soiffer R, Freedman A, Mauch P, Ritz J, Nadler L and Anderson KC. Mono clonal-antibody purged bone marrow transplantation therapy for multiple myeloma. Leuk Lymphoma 1995;17:87.
38. Reece DE, Shepherd JD, Klingemann HG, Sutherland HJ, Nantel SH, Barnett MJ. Spinelli JJ and Phillips GL. Treatment of myeloma using intensive therapy and allogenic bone marrow transplantation. Bone marrow transplant 1995; 15:117-123.
39. Couban S, Stwart AK, Loach D, Panzarella T and Meharchand J, Autologous and allogenic transplantation for multiple myeloma at a single centre. bone marrow transplantation 1997;19:783-789.
40. Schiller G, Vescio R, Freytes C, Spitzer G, Sahebi F, Lee M, Wu CH, Cao J, Lee JC, Hong CH, Lichtenstein A, Lill M, Hall J, Berenson R and Berenson J. Selection of CD 34 + cells. Transplantation of CD 34 + Peripheral blood progenitor cells after high dose chemotherapy for patients with advanced multiple myeloma. Blood 1995; 86:390-397.
41. Bjork Strand B, Ljungman P, Svensson H, Hermans J, Alegre A, Apperley J, Blade J, Carlson K, cavo M, Ferrant A, Goldstone AH, Laurenzi AD, Majolino l, Marcus r, Prentice HG, Remes K, samson D, Sureda A, Verdonck LF, Volin L and Gafhrton G. Allogenic bone marrow transplantation versus autologous stem cell transplantation multiple myeloma-a retrospective case matched study from the European group for Blood and marrow transplantation. blood 1996; 88:4711-8.
42. Hartman O, Corroller AGL, Blaise D, Michon M, Phillip I, Norol F, Janvier M, Pico JL, Baranzelli MC, Ribie H, Coze C, Pinna A, Meresse V, Benhamon E, Peripheral Blood stem cell and Bone marrow transplantation for solid tumors and Lymphomas: Hematologic recovery and costs: Ann intern Med.: 1997; 126:600-607.
43. Faucher C, Le Coroller AG, Blaise D, Navakovich G, Manonni P, Moatti JP, maraninchi D. Comparison of G. CSF primed blood progenitor cells and bone marrow auto transplanation: Clinical assessm,ent and cost effectiveness. Bone marrow transplant, 1994; 14:895-90.
44. Uye-de Groot CA, Richel DJ, Rutten FF. peripheral blood progenitor cell transplantation mobilised by filgastrim; a less alternative to autologous bone marrow transplantation. Eur J. Cancer 1994;30A:1631-35.
45. Tricot G, Jagannath S, Vesole D, Nelson J, tindle S, Miller L, Cheson B, Crowley J and Barlogie B. Peripheral blood stem cell transplantation for multiple myeloma identification of favourable variables for rapid engraftment in 225 patints. Blood 1995;85: 588-396.
46. Mariette X, Fermand JP and Brouet JC. Myeloma cell contamination of peripheral blood cell grafts in patients with multiple myeloma treated by high dose therapy. Bone marrow Transplant 1994;14:47-50.
47. Vora AJ, Toh CH, Peel J and Greaves M. Use of G. CSF for mobilising peripheral blood stem cells: risk of mobilising clonal myeloma cells in patients with bone marrow infiltration. Br J Haematol 1994;86:180-182.
48. Corradini P, Voena C, Astolfi M, Ladetto M, Tarella C, Boccadoro M and Pileri A. High dose sequential chemoradiotherapy in multiple myeloma; residual tumour cells are detectable in bone marrow and peripheral blood stem cell harvess and after autografting. Blood 1995;85:1592-1602.
49. Raje. N, Powles R, Horlton C, Millar B, Shepherd V, Middleton G, Kulkarni S, Eisen T, Mehta J, Singhal S and Treleaven J; Br. J of Cancer 1997; 75(11): 1684-1689.
50. Harousseau JL, AttalM, Divine M, Milpied N, Marit G, Leblond V, Stoppa AM, Bourhis JH, Caillot D, Boasson M, Abgrall JF, Facon t, Colombat P, Cahn JY, Lamy T, Troussard X, Gratecos N, Pignon B and Auzanneau g, Bone marrow Transplantation, 1995;15:963-969.
51. Dilber MS, Abedi MR, Bjorkstrand B, Christensson B, Gahrton G, xanthopoulos KG and Edward Smith CI, Suicide gene therapy for plasma cell tumors. Blood 1996;88:2192-2200.

FUNCTIONAL CONSTIPATION-PHARMACOLOGICAL AND NATUROPATHIC PERSPECTIVES

G.Nabi Mir, B.Sc., M.Pharm, MBA, Ph.D.

Epidemiology

Constipation is a symptom rather than a disease and therefore, represents a subjective interpretation of a real or defined as a frequency of defecation of twice weekly or less on basis of large population, frequency alone is not sufficient criterion. Many constipated patients complain of excessive straining or discomfort at defecation, although the frequency of defection is within the normal range. This broad and essentially subjective constellation of symptoms has contributed to some confusion concering the incidence, pathogenesis, and treatment of constipation and defecation disorders.

Pathophysiology

Constipation may be regarded as a disordered movement through the colon and/or anorectum, although this does not occur in all patients who consider themselves constipated. Slowing of colonic transit occurs as a primary motor disorder in association with many diseases (Table 1) or as an adverse effect of many drugs. (Table 2) Diseases associated with constipation include neurological, metabolic and endocrine disorders and obstructing lesions of the gastrointestinal tract. In those patients in whom colonic transit is normal, various factors such as psychological and emotional may be the cause. Many classes of drugs (Table 3) are associated with constipation as the main side effect. Constipation is often present in patients with irritable bowel syndrome. It is differentiated from idiopathic constipation by the presence of abdominal pain in the lower abdomen, by the passage of small hard stools often, with the sense of incomplete evacuation, and by passage of mucus.

Table-1: A Patient not taking laxatives complains of two or more of the following for at least 12 months:

1. Straining with at (east 25% of bowel movements.
2. A feeling of incomplete evacuation with at least 25% of bowel movements.
3. Hard or pellet stools with at least 25% of bowel movements.
4. Stools less frequent than three per week.

B. Potient has fewer than two bowel movemenbts per week on average for at least 12 months.

Table-2: Diseases associated with chronic constipation

Neurogenic Disorders
Autonomic neuropathy
Diabetes mellitus
Hirshcprung's disease
Intestinal pseudo-obstruction
Multip[le sclerosis
Parkinson's disease
Spinal cord injury
Nonneurogenic disorders
Hypothyroidism
Hypercalcemia, Hypocalcemia
Panhypopituitarism
Systemic scalerosis

Table-3: Drugs associated with Constipation

Anticholinergics
Anticonvulsants
Antidepressants and Psychotherapeutic drugs
Antihypertensives
Antiparkinsonian drugs
Calcium channel blockers
Diuretics
Opiates
Cation-containing agents
Alumunium (antacides, sucralfate)
Bismuth
Calcium (antacids, supplements)
Iron supplements

Diagnostic Tests in the Adult Patients.

Initial evaluation incorporates a careful history with particular attention to identify potential risk factors. This includes defining the nature and duration of the complaint. It is helpful for patients to record their bowel habits and food intake for several weeks. A recent persistent change in bowel habits, if not associated with a readily definable cause of constipation, should prompt an evaluation to exclude structural bowel causes or organic diseases^2. Only after such diseases have been excluded should a diagnosis of functional constipation, using following tests, be considered:

Studies of colorectal structure.

Flexible Sigmoidoscopy and Colonoscopy

JK-Practitioner 1999; 6(4):270-272
From the Department of Drug Research Laboratories, Inc. Buckingham, USA (Mir)
Received July 1999 Accepted July 1999

Correspondence to : G.Nabi Mir, B.Sc. President & CEO Drug Research Laboratories, Ind. P.O.Box 394, Buckingham, PA 18912, USA.

Barium Radiography
Studies of Colrectal Function
Radioopaque Marker Studies
Anorectal Manometry
Defecography

Drug Therapy

The management of functional chronic constipation includes patient education, behavior modification, dietary changes and, as Table 4 indicates judicious use of laxatives.

Pharmacological agents to promote colonic transit by increasing colonic motor activity have proved disappointing[3]. Agents such as bethanechol and neostigmine have been tried with little success and may be associated with adverse effects. Prokinetic agents such as metoclopromide and cisapride are ineffective in most severely constipated. Several drugs appear to be promising in refractory patients. Misoprostol has been successfully used in dosage of 600 ug one to three times daily. Another approach is use of polyethylene glycol/ electrolyte solution in dose range of 8 to 24 oz daily. Finally a recent report suggest that colchicine, 0.6 mg three times a day may be efficacious in patients with severe colonic intertia[4].

Table-4: Laxatives for the Management of Constipation

Lasative	*Usual Adult Dose*
Bulk Forming laxatives	
Natural (e.g. psyllium)	7 g/day
Synthetic (e.g. methycellose, polycarbophil)	4-6 g/day
Emollient Laxatives	
Mineral oil	15-45 ml/day
Hyperosmoler Laxatives	
Polyethylene glycol	8-24 oz/day
Lactulose	15-30 ml/day
Sorbitol (70%)	15-30 ml/day
Glycerin	3 g suppository
Saline Laxatives	
Magnesium	2400 mg (30ml)
Magnesium citrate	200 ml
Stimulant Laxatives	
Castor oil	15-60 ml
Diphenylmethanes	
Phenolphthalein	65-130 mg
Bisacodyl	30 mg; 10 mg suppository
Anthraquinones	
Aloe (casanthrol)	30-60 mg
Cascara sagrada	2-5 ml
Senna	17-34 mg

Table-5: Naturopathic Therapies for Constipation

Therapy	Dosage	Adverrse Effects
Water	6-8 glasses/day	None
Fiber		
Flax seed	1 T of whole or crushed seed 8 glasses of water 2-3/day	None
Psyllium seed husk	12-40 g daily	Rare
Dietary (seeds, nuts whole grains, vegetabls, fruit)	2-3 servings/day	None
Senna (dried leaves or pods)	0.5-2 g/day (1 t=1.5g) or 20-60 mg sennosides/day	Intestinal Colic
Magnesium sulfate	120-700 mg elemental Mg/day	Rare: Kidney Damage

Conclusion

Most patients with chronic constipation may not always respond to the above pharmacological interventions. Other options include naturopathic approach, which is discussed below.

Naturopathic Perspective

Causative Factors

A important concept in understanding constipation is that it is a symptom, not a disease. This realization necessitates investigation for the causative factors of constipation. These causes vary case by case; thus the management of constipation is inclusive of many types of interventions. Inadequate fiber in diet and poor fluid intake are widely accepted as the most common causes of functional constipation (table 5). Lack of fiber in diet prevents stool bulking which manifests as decreased mechnical stimulation for persitalsis. Another important cause of constipation is lack of exercise. A sedentary lifestyle results in altered autonomic nervous function which in turn, results in a dynamic colonic motility[5]. These causes are by far the most common contributing factors to the development of constipation, and as such, should be addressed.

Holistic Diagnosis

Successful treatment of constipation demands a thorough investigation. A complete history of defecation must be obtained. Additionally, a survey of the patient's diet is important to determine whether lack of dietary fiber or water, food allergies, of quantities are contributing factors. Life style habit such as exercise, means of relaxation, smoking and caffeine play role in gastrointestinal health and functioning. The emotional well being of the patient is an important area of inquiry, because depression and stress can contribute to the development of constipation. Further physical examination may uncover signs of endocrine or neurological disorders as well as functional disorders of the anus[6]. The naturopathic approach to treatment is based on the premise of identifying and treating the cause of the constipation. Lack of dietary fiber, low fluid intake, and insufficient exercise remain the most common causes.

Table-6: Classification of Laxatives

Criterion	Classification
Origin	Plant
	Synthetic
Intensity	Drastic
	Purgative
	Laxative
	Aperient
Site of Action	Small intestine
	Large intestine
	Entire bowel
Chemical structure	Salts
	Sugars and sugar alcohols
	Bulking agents
	Anthraquinone derivatives
	Diphenylmethane derivatives
	Fatty acids
	Bile acids
	Docusate sodium
	Benzamides
Mode of action	Osmotic
	Bulking agents (dietary fiber)
	Bowel stimulants, irritants
	Antiabsorptive, secretogogue
	Contact Laxatives
	Prokinetic
	Lubricants
	Lubricants
	Fecal softeners
	Rectal evacuation aids.

Laxative Therapy

There are a variety of laxative agents effective in the treatment of constipation (table 6). Effective laxatives can be used in the naturopathic setting include anthraquinone-containing herbs and magnesium. The anthroquinone-containing herb are Aloe, Senna, Cascara. Frangula, and Rhubarb. The most widely used anthraquinone used is senna. The senna derivatives are known as sennosides. The sennosides are pharmacologically inactive (table 7) in the upper gastrointestinal tract and pass without effect into the large intestine where microflora metabolize the molecule into bioactive end products including sennidines. The effect of sennosides is primarily exerted by their effect via excessive secretion and accelerated transit time. The effect is exerted on nerve fibers on the intestinal wall, probably by release of prostaglandins[7]. Magnesium sulfate is poorly absorbed and hence creates an osomtic effect. Furthermore, magnesium is a known smooth muscle relaxant. In case of spastic constipation, magnesium is ideal therapeutic agent[8].

Conclusion

From the preceding discussion it is evident that identification of all contributing factors is important. The least harmful therapies are used first. Patient education regarding healthy lifestyle choices and self-responsibility is paramount. Finally successful treatment of constipation is usually multifaceted.

References:

1. Floch MH, and Wald A. Clinical evaluation and treatment of constipation. Gastroenterologist. 1994; 2: 50-60.
2. Read NW, and Timms JM. Defecation and Pathophysiology of constipation. Clin Gastroenterol 1986;15:937-965.
3. Wald A. Clonic and anorectol motility testing in clinical practice. Am. J Gastroenterol 1994;89:2109-2115.
4. Wald A. Evaluation and Management of Constipation. Clin. Perspective in Gastroent. 1998;107-115.
5. Alschular LN. Naturopathic perspective on Functional constipation. Clin. Perspective in Gastroent. 1998;128-133.
6. Cheskin II, Kamal N, Crowell MD. Mechanism of constipation in older patients and effects of fiber compared with placebo. J Am Geriatr Soc. 1995;43:666-669.
7. Frexions J, Staumour G and Fioramonti JN. Effects of sennosides on colonic myoelectrilcactivity in man. Dig Dis Sci 1989;34:214-219.
8. Murry M, and Pizzorno J. A text book of natural medicine. Bothell WA: Bastyr University, 1998.

NON-PSYCHIATRIST CLINICIANS TRAINING IN PSYCHIATRY, ITS PERCEIVED ADEQUACY AND MODALITIES OF TREATMENT USED.

M. Margoob M.D; Mohammed Maqbool Dar M.D.; Mir Manzoor Ahmad M.D.; Arshid Wani MBBS.

Abstract : A survey of 71 expert non-psychiatric clinicians was carried out to find out their usage of different treatment modalities for the management of psychiatric diseases, their duration of training in psychiatry and its perceived adequacy as well as referral patterns. This was done using a specially designed self-report comprehensive proforma. Majority of these clinicians treated their patients pharmacologically with antidepressants and anxiolytics; almost all of them felt that they had been inadequately trained in psychiatry and that they required more training. Non-pharmacological modalities of treatment were infrequently employed. The internists tended to manage their psychiatric disorder patients themselves while as the other specialists tended to refer their patients for specialist care. Important implications for care and need for improving undergraduate and postgraduate teaching in psychiatry are discussed. Implications for health care planners are enumerated.

Key words: Non-psychiatric clinician, Treatment modalities, Consultation-liaison,

JK-Practitioner 1999; 6(4):273-277

Introduction:

The widely read Davidsons Principles and Practice of Medicine, an undergraduate textbook of internal medicine reports on the prevalence of psychiatric disorders in the united kingdom in different populations as follows[1]:

Community	:	15-20%
General practice attenders	:	30%
General hospital outpatients	:	20-30%

Indian figures for depression in primary care or medical settings range from 4.3% to 39.3%[2,3,4]. Western estimates for depression in primary care range upto17%[5,6,7]. One study estimated that around 50% of outpatient cases in a general hospital suffer psychiatric disease serious enough to warrant consultation[8] and out of these only 4% are referred for specialised consultation and management[9]. Figures for any psychiatric disorder from other developing countries include 19.6% of children in a paediatric care clinic in Nigeria, 53% of outpatient attenders in a poor urban area of Chile, and 37.6% of elderly general practice attenders in Brescia, Northern Italy which is a relatively underdeveloped region[10,11,12]. Exact figures from general hospital attenders in kashmir valley are not available but the incidence of depressive disorders has been found to have increased with only 203 patients with depression being registered in 1971 compared to 409 in the year 1989[13]. These figures go to show that worldwide immense human suffering ensues because of depression and other psychiatric illnesses. Unfortunately physicians often tend to miss the diagnosis. Amin and others[14] report that almost two-thirds of cases of depression in a primary care setting were missed by the treating physicians. Paykel and Priest[15] report that nearly half of the cases of depression were missed by primary care physicians in the UK. They also report that patients are more likely to consult a physician for their problem rather than seek specialist care from a psychiatrist.

Undergraduate training in psychiatry in the Government Medical College, Srinagar, as in most medical colleges in India, includes three weeks of posting at the Government Hospital for Psychiatric disease, ten theory classes and students have to answer a five marks question during their final year examinations. There is also a short assessment during the viva-voce examination held in the final year. Comparably for the United States Medical Licensing Examination Steps I, II and the clinical skills assessment, the content from psychiatry and the behavioural sciences may be as high as 20% with assessment in psychiatric history taking, diagnosis, and principles of management. Although data for post-graduate training in our state in the specialities of general medicine, paediatrics, and neurology are not available, they do not appear to have a psychiatry rotation at all.

From the Department of Pshychiatry Govt. Medical College Srinagar Kahmir India (Margoob, Ali, Dar, Ahmad Wani)

Received August 1999 Accepted September 1999

Correspondence to : Dr. Mushtaq A. Margoob POBox No. 701, GPO, Srinagar Kashmir.

Medical students and residents tend to use diagnostic categories which are obsolete and which have no psychiatric currency[16].

The present study was undertaken with the objective of finding out the training imparted to non-psychiatric clinicians, its perceived adequacy, their own feelings about it and the extent of psychiatric morbidity seen and treated by them.

Material and Methods:

A questionnaire specially designed for such type of studies was used[17,18]. In addition to socio-demographic data the questionnaire consisted of various items divisible into nine groups. The first group consisted of the items referring to the frequency of psychiatric morbidity and the opinion of clinicians regarding causation of psychiatric crisis. The second group consisted of nine items referring to clinician methods of treating psychiatric disorders. The third group consisted of six items covering various aspects such as reasons, and frequency of referral sought by clinicians in their patients having psychiatric illnesses. The fourth group of items referred to the opinion of these clinicians about the adequacy of under-graduate psychiatric training that they had. The other question groups included their opinion regarding the causation of psychiatric morbidity and the attitudes of clinicians towards psychiatric patients.

A total number of 134 clinicians could be contacted. They were requested to return the filled up questionnaires without any further reminders. The doctors were contacted again if they did not return the questionnaire within one month. One more request at a later date (three requests in total) was made to return the filled- up questionnaire. Statistical averages were calculated and tabulated.

In an earlier communication we had reported on the findings about the non-psychiatrist clinicians attitudes towards psychiatric illnesses and psychiatric patients[18]. The findings about the clinicians training in psychiatry, its perceived adequacy, their use of drugs and other management techniques, as well as referral patterns are reported here. Implications for resource allocation and training are discussed.

Results:

53% of the surveyed non-psychiatric expert doctors returned the filled up questionnaire; the majority of them being faculty members of the Government Medical College, Srinagar and most of them being available to their patients at hospital off hours. A brief description of the sample and socio-demographic data are presented in table 1. As is obvious the majority were males, most of them were past the age of 40 years and a large majority had been in clinical practice for a period greater than 10 years. Most (88.06%) of them used anxiolytics and antidepressants to treat psychiatric illnesses; antipsychotics and other drugs being used much less often. Other methods used and reported by the clinicians include "placebo, supplementation of food, reassurance, behavioural modifications etc.". Table 2 shows a more detailed break up of the methods employed. As regards the perceived adequacy of clinicians training and treatment methods, a sizable proportion (29%) reported being unsatisfied with their own treatment of such cases and 12% said that the response of such patients to treatment was poor. More than a quarter reported having had no formal training at all in psychiatry, 15% reported one month of training and only 17 said that they had received training for greater than a month. A great majority (85%) of the surveyed clinicians reported that they would have benefited from further training and wanted to know more about psychiatry. This included two people who had received training for 2 years in the discipline of psychiatry but still perceived it as inadequate. Table 3 shows the most common reasons for referral of cases to a psychiatrist, the most common being an excited and unmanageable patient, to confirm diagnosis and treatment, and for "better" management.

Discussion:

The current study assumes great significance when viewed against the backdrop of a ten fold increase in the number of psychiatric cases seen in the out patient department of the Psychiatric Diseases Hospital, Srinagar over a short period of 5 years[19]. 69 of our surveyed experts reported seeing psychiatric patients in their practice and this group compromised 25% of their practice. Amongst these, the general practitioners (GPs) treated about a quarter of such cases themselves while most of the experts reported that they referred their patients for speciality care although such cases are few and far in between. Considering the report of Amin and others [14] wherein they say that primary care physicians missed the psychiatric diagnosis in two-thirds of cases, the actual number of cases seen and missed by non-psychiatrists could be overwhelmingly high. It is a well-established fact that undiagnosed psychiatric morbidity results in prolongation of the patient's distress, unnecessary investigations and consequent increases in health care costs[20]. Major depression is also a part of cancer (20%), post MI (20-50%), stroke (25-50%) with mortality in the post MI patient at 4 months being seven times higher among those with concurrent depression[21]. It is now recognised that one third of the contribution to the Disability Adjusted Life Years (DALY's) is dependent on only the behaviour of individuals[22]. Some of these behavioural difficulties include impaired socio-occupational functioning, increased medical service utilisation, increased alcohol and other substance related morbidity, suicides, disruption of the fabric of the family etc.

Our surveyed clinicians reported treating patients mostly with reassurance and tranquilisers as also referral to specialist care by a psychiatrist. Only a small minority (15%) reported treating such patients with other modalities like counselling and psychotherapy. None reported the use of psychosocial interventions like listening, emotional support, relaxation, family support, meditation, or cognitive therapy all of which can be practiced by primary care and non-mental health medical professionals in combination with medicines[23]. The use of anxiolytics is wide spread with half of the surveyed clinicians reporting their use. A few studies have found that the personal use of benzodiazepines by a physician, rather than rational medical decision making, tends to increase the proneness to prescribe these drugs[24]. Also short acting and ultra-short acting benzodiazepines are the most commonly used hypnotics, are used more frequently by GP's rather than psychiatrists, are used most for sleep induction in the elderly and in women, and tend to be used for prolonged periods once they are prescribed[25]. Although dosages and classes of drugs used were not specifically asked for, the overtendency to prescribe benzodiazepines is disturbing, what with the very high potential for abuse and development of dependence on these agents. Use of these drugs beyond six weeks is generally unsafe and would require expert care by a psychiatrist. As mentioned earlier 29% of these clinicians were unsatisfied by their own treatment of such patients, but only 12% reported that the response of their psychiatric cases to treatment was poor. This discrepancy may indicate perhaps greater dissatisfaction than reported as in a later section of the questionnaire. 85% of these clinicians reported feeling inadequately trained in psychiatry. There were a few other interesting discrepancies. When asked about reasons for referral to a psychiatrist, 99% gave one or more reasons but out of them 23% had, in an earlier question, said that they did not refer patients to a psychiatrist at all! In the reasons for referral section the same question was repeated twice as can be seen in table 3, but the responses are different. Eleven people said yes to this question the first time but again four gave their assent when the question was repeated.

As recorded earlier, the great majority of these experts reported feeling that their psychiatric training was inadequate. All eighteen doctors from the speciality of medicine and all five from paediatrics had not amazingly received any training in psychiatry during their post graduate residencies. Compare this with a recent study of internal medicine residencies in the USA[26] wherein only 25% of the directors of such residencies reported feeling satisfied with the six month formal period of such training particularly in the areas of somatoform disorders, psychotropic drugs and office psychotherapy! About 40% of British general practitioners train formally in a psychiatric post and still feel inadequately trained in terms of drug treatment and management of excitement.[27] which is highly relevant when we find that 42% of our surveyed experts reported excitement (see table 3) as a reason for referral. There is thus a great need for increasing the duration of psychiatric training at both the undergraduate as well as the post-graduate level, which has been demonstrated to increase the efficacy of non-psychiatrists to detect and treat psychiatric morbidity[28]. The defeat depression campaign run by the Royal College of Psychiatrists from 1992 to 1996 resulted in 40% of GP's changing their practices of diagnosing and managing depression for the better[29]. A study done in the Netherlands found that general practitioners who had been trained in the recognition and treatment of psychiatric illnesses treated depression better than those without such training and in fact their patients recovered faster than the other group[30]. In fact the GP has a very important "gatekeeper" function in the pathway to specialised psychiatric services for the more disabled patients. The neglect of psychiatric training thus results in considerably greater distress, morbidity, man-days lost at work, inefficient utilisation of health care resources and consequent increase in health costs and the burden to society. The proportion of people in psychological crisis, as perceived by our surveyed experts, has increased four fold in the last 10 years and they are inadequately trained to handle such crisis. If an internal medicine resident does not receive training in psychiatry, the question of utilising the protocols and philosophies of emergency psychiatry hardly arises. This aspect is another important area for which data was collected in the present study and which will be reported separately by the authors .

The sub-speciality of consultation-liaison psychiatry assumes a special significance in such a situation. While the consultation part of this branch is widely practiced in our country, liaison work tends to be neglected. It refers to the process of assisting and teaching non-psychiatric health professionals like physicians and surgeons about psychosocial and psychiatric problems occurring among patients under their care[31]. The mental health professional is attached to a medical ward or a special unit and he or she attends clinical rounds everyday with the treating team and the accent is on teaching the non-psychiatric expert[32]. General hospital psychiatry in India however remains based on consultation work and our limited resources may allow us only the "luxury" of a psychiatric consultant running regular outpatient and inpatient units. It has been an irony that inspite of the great keeness of the founders of the prestigious Sher-I-Kashmir Institute of Medical Sciences of the state, a department of psychiatry could never get established. The steps taken by the present authorities of this institute to start a general hospital psychiatry unit in the under graduate medical college associated with it is laudable and could prove a welcome step. This would go a long way in realising the goal of the visionaries associated with the founding of the institute who in the starting phase even advertised the posts for the department of psychiatry. If properly established such a unit would hold great promise in facilitating liaison work with non-psychiatrist clinicians. A continuing medical education program in psychiatry for the general practitioner could also be devised.

The role of counselling, and the teaching of such counselling techniques may again be facilitated by such consultation-liaison opportunities. Counselling remains a much maligned, misunderstood word described as " a trendy panacea for a variety of problems" [33]. It means not only to help the client explore, discover and clarify ways of living more resourcefully but also to offer insight and understanding so that patients help themselves rather than listen to the directives of others. This is in contrast to how non-psychiatrists regard it as meaning education about the illness, problem solving, advice about drugs etc. Patients with chronic psychosis like schizophrenia tend to visit general care practitioners more often than even diabetics do (9.5 visits per year vs. 7.7 visits per year) and up to 25% of such patients can be managed by the GP after dropping out of psychiatric care[33]. Focus and organisation in the care of such patients and counselling, so that drug compliance increases, can be improved by the development of care packages and brief protocols of management in consultation with the specialist psychiatrist.

Results of the present study strongly suggest that the kind of training received at the undergraduate and post-graduate level is insufficient to manage psychiatric patients properly. Undergraduate students hardly get to encounter the kind of cases that they are likely to see in their later careers and disciplines like child psychiatry, emergency psychiatry, geriatric psychiatry are unlikely to be even mentioned. They may at the most spend 2-3 hrs per day in psychiatry for about 3 weeks throughout 2000 days of their professional training. Medical students do not take subjects like dermatology, radiology and psychiatry seriously since there are no examinations for these subjects[17]. To worsen the situation, the Medical Council of India in its 1997 review decided to reduce the medical interns posting in psychiatry to the status of just one of the three optional postings such that the intern can opt to miss psychiatry entirely if he so chooses [34]. A radical reappraisal of undergraduate as well as postgraduate training in psychiatry appears to be the need of the hour not only in our valley but throughout India as well. The lack of even a short posting for postgraduates is particularly appalling and needs urgent remediation. Policy makers and medical education supervisors need to take particular note. A largely remediable psychological burden will continue to hamper the social, occupational and educational functioning of a huge number of patients with psychiatric illness unless public health planning is radically restructured. A second related concern is the function of primary care as a first filter in the detection and management of psychiatric morbidity. Governments in several of the underdeveloped nations are shifting health care resources to the development and strengthening of primary health care because it is cheaper, easier to implement and most importantly, more efficient. What is essential to realise is that the two above-mentioned factors go hand in hand. Strengthening of primary care has to be accompanied by determined efforts to improve the skills of the primary care physician as well as provide support for effective management.

References:

1. Loyd GG, Psychiatr. Edwards CRW, Boucnier IAD, Haslett C, Chilvers E Eds, Principles and practices of (medicine. Edingburgh, Churchill Livingstone, 1995;978.
2. Bagadia VN, Ayyar KS, Lakdawala PD, SM, Acharya VN, Pradhan PV, Psychiatric morbidity among patient attending medical out patient departments. Indian Joumal of Psychiatry 1986;28:139-144.
3. Sriram TG, Shamsunder C, Mohan K; Shanmugam V, Psychiatric Morbidity in the medical outpatients of a general hospital. Indian Journal of Psychiatry 1986;28:325-328.
4. Bhatia MS, Balkrishna, Dhar NK, Bohra N, Gupta H. Malik SC, Psychiatric Morbidity in patients attending medical OPD. Indian Journal of P)sychiatry 1987;29:243-246.
5. Hoeper EW, Nycz GR, Cleary PD, Regier, Goldberg ID, Estimated Prevalance of RDC mental disorder in primary medical care. International Journal of Mental Health 1979;8:6-15.
6. Blacker CVR, Clare AW, Depressive disorders in primary care. Br J Psychiatry 1987;150:737-751.
7. Dhadphala M, Cooper G, Cartwright-Taylor L, Prevalence and presentation of depressive illness in a primary health care setting in Kenya. Am J. Psychiatry 1989;146:659-661.
8. Lipowski ZJ, Review of consultation psychiatry and psychoosomatric medicine: clinical aspects. psychosomatic

Med 19767;29:201-224.

9. Lipowski ZJ, Wolston EJ, Liaison Psychiatry: referral patterns and their stability over time: Am J Psychiatry 1981;130:1608-1611.
10. Gureje O, Omigbodun OO, Grater R, Acha RA, Ikuesan BA, Morris J, Psychiatric disorders in a paediatric primary care clinic. Br J Psychiatry 1994;65:527-530.
11. Araya R, Wynn R, Leonard R, Lewis G, Psychiatric morbidity in primary health care in Santiago, Chile. Br J Psychiatry 1994;165:530-533.
12. Turrina C, Caruso R, Este R, Lucchi F, Fazzari G, Dewey ME, Ermentini A, Affective disorders among elderly general practice patients. Br J Psychiatry 1994;165:533-537.
13. Margoob MA, Beig AA, Dutta KS, Depressive disorders in Kashmir. JK Practitioner 1995;p2:22-24.
14. Amin G, Shah S, Vankar GK, The prevalence and recognition of depression in primary care. Indian Journal of Psychiatry 1998;40:364-369.
15. Paykel ES, Priest RA, Recognition and management of depression in general practice. Br Med Joumal 1992;305:1198-1202.
16. Bombana JA, Ferraz MP, Mari JJ, Neurovegetative dystonia - psychiatric evaluation of 40 patients diagnosied by general physicians in Brazil. J Psychosom Res 1997;43:489-95.
17. Chadda RK, Shoma S, Psychiatric aspects of clinical practice in government hospitals: A survey of non-psychiatric clinicians. Indian Journal of Psychiatry 1996;38:86-93.
18. Margoob MA, Mustafa T, Non-psychiatric clinicians attitude towards psychiatric disorders and psychiatric patients: a survey of 71 experts. JK Practitioner 1997;4:165-168.
19. Margoob MA, A study of present magnitude oof psychiatric disorders and existing treatment services in Kashmir (1990-94). JK Practitioner 1995;2:114-117.
20. Lipowski ZJ, Somatization: the concept and its clinical applications. Am J Psychiatry 1988;145:1358-1368.
21. Murthy RS, Editorial, Emergiing aspects of psychiatry in India. Indian Journal of Psychiatry 1998;40:307-310.
22. World Bank, World Development Report: Investing in Health. New York, Oxford University Press, 1993;
23. Snaith P, Meditation and Psychotherapy. Br J Psychiatry 1998;173:193-195.
24. Linden M, Gothe H, Speciality training and the personal use of benozodiazepines by physicians affect their proness to prescribe tranquilizers. Pharmacopsychiatry 1998;31:42-47.
25. Balestrieri M, Bortolomari M, Galletta M, Bellantuono C, Hypnotic drugs in a populatio: prescriptions by the specialist and the general practitioner. Recenti Prog med 1998;89:3-6.
26. Sullivan MD, Cole SA, Gordon GE, Hahn SR, Kathol RG, Psychiatric training in medicine residencies: current needs, practices and satisfication. Gen Hosp Psychiatry 1996;18:95-101.
27. Ratcliffe J, Gask L, Creed F, Lewis B, Psychiatric training for family dooctors: what do GP registrars want and can a frief coourse provide this? med Educ 1999;33:434-438.
28. Williams K, Self-assessment of clinical competence by general practitioner trainees before and after a six psychiatric placement. Br J Gen Pract 1998;48:1387-1390.
29. Rix S, Paykel ES, Lelliott P, Tylee A, Feeling P, Gask C, HDart D, Impact of a national campaign on GP education: an evaluation of the Defeat Depression Campaign. Br. J Gen Pract. 1999;49:99-102.
30. Ormel J, Tiemens BG, van Os TW, van der Meer K, Jenner JA, van den Brink RH, Improved recognition and treatment of depression with occasional faster recovery through post-graduate training of family practitioners. Ned Tijdschr Geneeskd 1998;142:272-2577.
31. Srinivasan K, General hospital psychiatry - an overview. John P, Joseph G eds, Clinical Psychiatry - recent trends. Ernakulam, Ernakulam Psychiatric Society 1993;53-63.
32. Greenhill MH, The development of liaison programs. Usdin G. ed., Psychiatric medicine. New York, Branner Mazel Inc. 1977;115-191.
33. Rowland N, Can general practitioners counsel? J.R. Coll Gen Pract Pract 1989-39:435.
34. Shamsunder C, who needs psychiatry, who cares for pschiatry? Indian Journal of Psychiatry 1998;40:305.

PRIMARY LYMPHOMA OF BONE - REVIEW OF 56 CASES

A. Gupta M.D.; D.P. Singh M.D.; S. Ghoshal M.D. D.N.B.; R. Jalali M.D.; R. Kapoor M.D.; S.C. Sharma M.D.

Abstract: *A review of total lymphoma cases treated at P.G.I. M.E.R., Chandigarh between year 1971-1988 was done. Out of 2360 cases of lymphoma, 1652 (70%) were N.H.L. and out of this a total of 56 cases (3.3%) constituted primary lymphoma of bone (P.L.B.). These cases were analysed in respect of their age and sex prevalance as well as site of presentation and type of histology. The primary modality of treatment was radiation. However chemotherapy was also added in 29 cases. These patients were then analysed for their local control and disease free survival as well as patterns of failure. The role for primary surgery is also analysed and discussed.*

Key words: *Primary bone tumors, Lymphoma, Radiotherapy.*

JK-Practitioner 1999; 6(4): 278-281

Introduction

Primary lymphoma of bone (PLB) is an uncommon condition constituting approximately 2 to 3% of all cases of malignant lymphomas. This condition was established as a distinct entity by Parker and Jackson in 1939[1], who reported 13 cases of PLB. Since then PLB has been studied extensively in relation to its histomorphological features, clinical behaviour, treatment and prognosis. However due to rarity of this condition, PLB still presents with diagnostic and therapeutic problems. Because of relatively late development of distant metastasis, this disease generally runs a slow clinical course and its prognosis is good as compared to malignant lymphoma involving other sites or other primary osseous malignancies. Radiation therapy plays an important role in the control of local disease and is considered to be the treatment of choice in these cases where the disease is localized to the site of origin. Chemotherapy is needed in locally advanced and disseminated cases.

We present 56 cases of PLB in this study to high light the clinical presentation, diagnostic problems, treatment and prognosis of this disease. Special emphasis has been laid to define the role of primary radiation therapy in the management of this disease.

Material and Methods

Between 1971 and 1988, a total of 2360 cases of lymphoma were diagnosed at PGIMER Chandigarh, Non Hodgkin's type constituted 70% (1652) of all cases. A total of 56 cases of PLB were seen during this period, there by, constituting 2.3% of all lymphoma cases and 3.3% of all non-Hodgkin's lymphoma cases. These cases were differentiated from secondary osseous involvement from disseminated non-Hodgkin's lymphoma according to the criteria laid by Coley et al. All the patients underwent a detailed clinical workup. The investigative workup included complete haemogram, renal and hepatic functions. Radiological investigation included plain x-ray of the involved bone, limited skeletal survey chest x-ray and bone scan. An open biopsy was done in all the cases. All the patients underwent bone-marrow examination to rule out the involvement. After complete workup, all cases were staged according to Ann Arbor staging system, for malignant lymphomas.

Analysis of Material

Age and Sex: Table I shows the distribution of the patients according to the age group with peaks seen in third and fifth decades. The male to female ratio was 4.6 to 1 indicating the predominance of male involvement.

Table - I: Age and Sex Distribution

Age (in years)	Male	Female	Total
10-19	3	0	3 (5.3%)
20-29	12	2	14 (25%)
30-39	5	4	9 (16%)
40-49	16	2	18 (32%)
50-59	5	1	6 (10.7%)
60-69	3	1	4 (7.1%)
70-79	2	0	2 (3.5%)
	46	10	56 100%

Anatomic Sites: Table II shows the anatomical distribution of the cases. Both long as well as flat bones

From the Department of Radiotherapy, Post-graduate Institute of Medical Education and Research Chandigarh India
(Gupta, Singh, Ghoshal, Jalali, Kapoor, Sharma)

Received August 1998 Accepted March 1999

Correspondence to : Dr. A. Gupta, H.No. 266, Krishna Nagar, Jammu - 180 001.

were involved with equal frequency (28 in each case).

Table -II: Long Bone distribution:

		Rt.	Lt.	Total
1.	Femur	4	6	10
2.	Humerous	5	3	8
3.	Tibia	5	3	8
4.	Clavicle	0	1	1
5.	Radius	1	0	1
		15	13	28

Flat Bone Distribution:

		Rt.	Lt.	Total
1.	Ileum	9	7	16
2.	Scpula	2	3	5
3.	Occipital	2	0	2
4.	Calcaneum	1	0	1
5.	Metatorsal	1	0	1
6.	Sacrum	1	0	1
7.	Vertebra	1	0	1
8.	Rib	1	0	1
		18	10	28

Clinical Presentation: Pain at the local site was the most common symptom noted in 95% of cases. Associated soft tissue swelling was equally common, seen in 91% cases. Size of the soft tissue swelling was recorded on physical examination. Eleven patients had associated swelling less than 5 cm. In 30 patients, the size of swelling ranged between 5 and 10 cms and in 10 patients there was big soft tissue swelling measuring more than 10 cms. Two patients (3.5%) presented only with persistant pain. Pathological fracture was the mode of presentation in 2 patients (3.5%), while 1 patient (1.7%) presented wih cord compression symptoms (paraplegia) due to primary involvement of vertebra. Duration of symptoms varied from 2 to 24 months with an average of 10 months indicating late hospital presentation in majority of the cases.

X-ray Appearance: There were no pathognomonic roentgenologic features of this tumor noted in the present series. In long tubular bones, the location was mostly in diaphysis. The cortical destruction was seen in the form of permeative, moth eaten or5 frankly destructive appearances. The overall appearance of cortical involvement was osteolytic, but in a significant number of cases a concomitant sclerotic lesion was also seen, thereby, presenting a mixed picture of osteolytic and osteoblastic involvement. Associated soft tissue mass was seen in most ofthe cases. Two cases revealed pathological fractures in addition to the destructive lesions. The involvement of the flat bones also showed the similar roentgenographic features.

Pathology: For histological sub-typing, Rappaport's classification was followed (table III). Thirty one patients (55.3%) were of diffuse histocytic variety. Ten patients (17,8%) belonged to diffuse histocytic-lymphocytic type. In 7 patients (12.5%), the histology was diffuse poorly differentiated lymphocytic while in 8 patients (14.2%), the histology was of unclassified nature.

Table III: Histological subtyping (Rappaport's Classification)

1.	Diffuse Histeocytic	31	(55.3%)
2.	Diffuse Histeocytic -lymphocytic	10	(17.8%)
3.	Diffuse poorly differentiated lymphocytic	7	(12.5%)
4.	Unclassified	8	(14.2%)

Clinical Staging: In 30 patients, the disease was localized to the primary site (stage IE) while in 26 patients, there were metastases to regional lymphnodes (Stage IIE).

Treatment

Radiation therapy was used as primary modality of the treatment, either alone or in combination with systemic chemotherapy. Of 56 patients in the present series, (25 44.6%) were treated by radiation alone, while in 29 patients (51.9%) radiation was combined with systemic chemotherapy. Two patients were treated with surgery and systemic chemotherapy.

Radiation therapy was delivered by megavoltage beam (cobalt 60 and 6 Mev linear acceleration). The radiation portals encompassed whole of the marrow cavity and a margin of soft tissue around the involved bone. The regional lymph nodes were also included into the field whenever enlarged. Radiation doses were between 35 to 50 Gys/20—25 fr. However, when systemic chemotherapy was combined, the radiation doses were kept towards lower side i.e. 35 Gy/3-4 wks.

Systemic chemotherapy was added along with radiation therapy in those patients who had extensive soft tissue involvemernt and those who had regional lymph node involvement. The chemotherapy regimes used were the standard CVP regime in 23 patients and CHOP regime in 6 patients.

Results of Treatment

The results are shown in Table IV. of 25 patients treated with irradiation alone, 19 (76%) achieved complete remission. Out of these 19 patients, 5 patients developed replase (local and distant), while rest 14 patients (56%) remained free of disease at the end of five years. 29 patients treated with combination of radiation therapy and systemic chemotherapy, 21 (72.3%) achieved complete remission. During followup of these 21 patients, 9 patients developed local or distant failures, thereby, achieving an overall control in 12 patients (41.3%) at the end of 5 years. The 2 patients treated with surgery and systemic chemotherapy have remained disease free at the end of 5 years. The overall 5 year disease free survival in all 56 patients was 50%.

Table IV:

Treatment Modality	Total	CR(%) number	Residual	Replase on FU	Over all controll rate at 5 years
1. Irradiation alone -	25	19 (76%)	6	5	14 (56%)
2. Irradiation+systemic Chemotherapy	29	21 (72.3%)	8	9	12 (41.3%)
3. Surgery + Systemic Chemotherapy	2	2 (100%)	0	0	2 (100%)
Overall 5 year disease free survival : 50%					

Discussion

PLB is a distinctly rare disease. It accounts for approximately 3% of malignant lymphomas[2,3]. Males are affected more often than females and the ratio of male to female occurence is 3:1[2,4]. Incidence is higher after second decade with a peak seen in fourth decade[5,6]. Pain, swelling and subsequent disability are cardinal clinical features[2]. Radiologically, bone destruction is a predominant feature, giving a mottled and patchy appearance[7]. Both lytic and blastic lesions may be seen in some cases. Histologically most of the cases have diffuse pattern with diffuse histiocytic variety being the most common type[7].

The treatment modality and the prognosis are entirely diferent in PLB as compared to the secondary bone involvement from dissseminated NHL. Therefore, it is very important to distinguish between the two Coley et al[5]., have laid down the following criteria for establishing the diagnosis of PLB:

1. Only a single bone is involved on prestation.
2. Unequivocal histology taken from the bony lesion.
3. Metastasis is regional on presentation or the onset of the symptoms of the primary tumour proceeded the appearance of metastasis by a period of at least 6 months.

PLB being a radiosensitive tumour, radiation therapy forms the primary modality of the treatment. Since the tumour spreads through the medullary cavity beyond the apparant involvement shown on the roentgenograms and often invades the soft tissues, radiation therapy must be given to a large field including the entire bone (from proximal to distal articular surfaces) and its soft tissue parts[8]. The regional lymph nodes must also be included into the treatment field if found to be significantly enlarged. A dose of 40 to 45 Gy in 4 to 4-1/2 weeks is the ideal dose for these tumours to achieve best control rates withacceptable morbidity[9]. Francis et al[6]. reported a 48% 5 year disease free survival in a group of 31 patients treated primarly be radiation therapy. In a review of 179 patients of PLB seen a Mayo Clinic[10], 5 year and 10 year survivals with radiation therapy were reported as 58% and 53% respecitvely. Wang[8] has reported a 5 year survival of 50% in 16 patients treated with radiation or surgery.

The use of surgery (in the form of amputation) for the local control of the disease is limited now and is reserved only for those cases which fail after radiation or when there is local recurrance after full doses of radiotherapy. This is because of the fact that radiation therapy gives equally good local control rates and at the same time entails no mutilation of the body. Boston et al.[11] reported in their series that those patients treated with excisions, amputation or resection combined with irradiation did not fare significantly better than those receiving radiation therapy alone after biopsy.

Systemic chemotherapy is reserved for locally advanced cases as radiation alone gives poor control rates in such cases. Involvement of regional lymph nodes and extensive soft tissue involvement form strong indications for the addition of systemic chemotherapy along with large field radiation. When chemotherapy is to be used, the doses of radiation are reduced by 5 to 10 Gy[12].

In the analysis of the prognosis in the present series, there was no relationship of age and sex to the prognosis. Associated soft tissue involvement had most significant impact over the control rates. Patients with extensive soft tissue involvement (more than 10 cms) had failure rate of 70% as compared to failure rate of 18% in cases with minimal soft tisue involvement. The poor prognosis was noted in flat bones (50% local failure rates as compared to 28.5%). The reason could be related to late presentation of cases and difficulty in delivering adequate radiation doses due to close anatomincal relationship to vital organs. Clinical stage of the disease also had an influence over the prognosis. Stage IIE had significantly high failurerates as compared to stage IE 1(57.8% vs. 23.3%). Among the histological subtypes, histiocytic variety had the best prognosis (22.5% failure rates) while other subtypes had higher failure rates (Histiocytic-lymphocytic: 57%, unclassified: 75%).

Conclusions

1. PLB is a rare disease 2. Majority of the patients presented late with soft tissue involvements. 3. Radiation alone to the whole bone is the best form oftreatemnt in early cases with minimal soft tissue involvement. 4. Systemic chemotherapy must be added along with radiation therapy for those cases with extensive soft tissue involvement and regional lymph node enlargement. 5. Type of bone, extent of soft tissue involvement, stage of disease and histology have impact over the prognosis.

References:

1. Parker F. and Jackson H.: Primary reticulum cell sarcoma of bone. Surg. Gynaecol. Obstet. 1939;68:45-53.
2. Dahlin DC. and Krishnan KU: Bone tumours, 4th Ed. Spring field IL, Thomas CC. 1986;208-226.
3. Rosenberg SA, Diamond HD, Jaslowitz B, and Grover LF. Lymphosarcoma: a review of 1269 cases. Medicine. 1961;40:31-84.
4. Singh DP, Dhillon MS, RK, Sharma SC, and Radotra BD.: Primary lymphoma of the bones of the foot: Management of two cases. Foot and Ankle. 1991;11:314-316.
5. Coley BL, Higinbotham NL. and Groesback HP: Primary reticulum cell sarcoma of bone. Radiology. 1950;55:641-58.
6. Francis KC, Higinbotham NL. and coley BL.: Primary reticulum cell sarcoma of bone. Surg. Gynaecol. Obstet. 1954;99:142-46.
7. Clayton MD, Butler JJ, Ayala AG, Ro JY. and Zomoga J: Pathologic and radiologic features withclinical correlates. Cancer. 1987;60:2494-2501.
8. Wang CC, and Fleischli DJ.: Primary reticulum sarcoma of bone with emphasis on radiation therapy. Cancer. 1968;22:9940998.
9. Mendenhal NP, Jones JJ, Kramer BS et al.: The management of PLB. Radiather. Oncol. 1987;9:137-145.
10. Ostrowski ML, Unni KK, Banks Pml. et al. Malignant lymphoma of bone. Cancer. 1986;58:2646-2655.
11. Boston HC, Dahlin DC, Ivins JC and Oupp RE: Malignant Lymphoma (so called reticulum cell sarcoma) of bone. Cancer. 1974;34:1134-37.
12. Moss WT. and Cox JD.: Raidation Oncology. Rationale Technique, Results, 6th Ed. Mosby CV. 1989;693-694.

With Best Compliments From

Nira Sons

Chinar Trust Building, Maulana Azad Road, Srinagar-190001

DISTRIBUTORS FOR:

☐ **Hoechst Marion Roussell Ltd.**
☐ **German Remedies Ltd.**
☐ **Fulford India Ltd.**
☐ **S.G. Pharmaceuticals Ltd.**
☐ **Group Pharmaceuticals Ltd.**
☐ **Wockhardt Ltd.**
☐ **Searle India Ltd.**
☐ **Sarabhai Chemicals Ltd.**
☐ **Raptakos, Brett & Co. Ltd.**

ANTI-CANCER DRUGS AND ANTI-RABIES VACCINE AVAILABLE

ATLANTO AXIAL DISLOCATION

M.A. Wani M.B., MS., M.Ch.; M.L. Babu M.S.; A.R. Kirmani, M.B. M.S.;
R.K. Saxena, M.B., M.S., M.Ch.; A.U.Ramzan M.B., M.S., M.Ch.

Abstract: *Because of its complexity, the mangement of patients with atlanto axial dislocation has always remained a challenge to the neurosurgeons. From 1982 to 1998, 31 patients with atlanto axial dislocation were managed by wiring the fusion with bone grafts. Most of the patients were in the age group of 25-55 years. In 5 cases the cause of subluxation was significant Crarnio Cervical Trauma. 5 cases had Atlanto-axial dilocation due to congenital causes which was aggravated by trivial trauma and 1 case was due to tuberculosis of the C2. The clinical features radiological findings and subsequent management of 31 cases of AAD treated with posterior wiring and fusion is discussed.*

The diagnosis was mainly radiological. All patients were put on cervical traction before surgical decompression and stabilisation was undertaken. This article deals with our surgical techniques and also illustrates many difficulties encountered while treating these patients. This paper also emphasises the importance of clinical, technical and biomechanaical principles which must be followed for a satisfactory stabilization.

Key words: *Atlanto axial dislocation (AAD) - Traction, CV Junction anomaly, Post. spinal stabilization and fusion, Trauma, Fracture Odontoid.*

JK Practitioner 1999; 6(4):282-285

Introduction

Malformations of the Atlanto Occiptal region have been recognised for many centuries[1]. Cranio-vertebral anomalies are the result of faulty develpment of the axial skeleton and of the enclosed neuro axis at the junction of the spine and the cranium. The clinical syndromes associated with these anomalies are attributed to: i) pressure on Neuro axis by bony abnormality ii) disturbance of CSF circulation and blood supply and iii) malformation of the nervous system.

The management of patient with Atlanto-axial dislocation remains complex and is a challenging problem to the Neurosurgeons[2]. Instability may be due to minor trauma sustained by patients who already have existing congenital anomaly. It may also be due to significant trauma sustained by the other wise normal atlantoaxial region and joint and it is also sometimes due to infections and degenerative diseases[2]. Since early 1990 a variety of surgical techniques (simple wiring, fixation, only bone grafting, methyl-meth-acrylate constructs, or a combination of bone grafts with wires, clamps, rods or screws) have been used to achieve atlanto axial stability[3]. We present a retrospective analysis of 31 patient with AAD trated with occipito cervical wiring and fusion. A tricortical bone graft from illiac crest was used graft in some cases and fibular graft was used in others. A tricortical bone graft is harvested from the posterior illiac crest. It has cortical surface available on three sides[13].

Material & Method

This study is based on analysis of 31 patients (1982-1998) who were diagnosed to have Atlanto axial dislocation and were subsequently managed successfully in the Department of Neurosurgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar. A majority of these patients were received in the Accident & Emergency area with history of Head Injury and Trauma to neck due to fall from cycle, scooter or tree. In one patient a heavy object had fallen over the posterior part of head. Table I shows various causes of Atlanto-axial dislocation. Most of the patients were males and in the age group of 25-49 years. Their mean age being 37 years. the youngest patient was 10 yearrs and the oldest 55 years of age. Table II summarises the clinical features of these cases. Radiological findings are analysed in table-III.

From the Department of Neurosurgery, SKIMS, Soura, Srinagar (India) (Prof. Wani, Baba. Kirmani, Saxena, Ramzan)

Received January 1999 Accepted September 1999

Correspondence to : **Prof. M.A. Wani, MBBS, MS; M.Ch., 15 Pamposh Colony, Natipora, Srinagar-190015, J&K, India.**

Table I: Atlanto-Axial Dislocation

Causes
◆ Significant Trauma = 25 cases
◆ Congenital (Minor Trauma) = 05 cases
◆ TB (C2 Minor Trauma) = 01 cases
Total = 31 cases

Table II: Altanto-Axial Dislocation

Symptoms/Signs	No. of cases
◆ Pain Neck	31
◆ Decreased R.O.M.	22
◆ Transient attacks of Paraesthesies	04
◆ Deformity of Neck	03
◆ Progressive Neurological Deficit	02
All complained of Pain Neck	

Table III: (Atlanto-Axial Dislocation)

(Plain x-ray Findings)	
◆ Fracture odontoid with subluxation C_1- C_2	07 cases
◆ C_1- C_2 subluxation only	19 cases
◆ Absent odontoid	02 cases
◆ Occ. atlas with subluxation	02 cases
◆ Destroyed C_2 (tuberculosis)	01 cases

Management

Twenty-five patients with history of significant trauma were received in the Casuality. All the patients had a quick review of air way circulation and neurological status. General systemic check-up was done to rule out associated injuries. All patients suspected to have neck trauma were put on a Cervical Collar. An X-ray study was performed on all cases in the emergency room. X-ray Cervical spine was done in neutral, flexion and extension to demonstrate injury to bones as well as to demonstrate subluxation of Atlanto axial Joint. It is not desirable to do stress films in fresh cases of Trauma. However, in certain situations the dislocation may not seem significant in Neutral Position. In those situations stress films are helpful to see mobility of the joint. However, an extremely cautions manipulation should be performed in order not to worsen a patient neurological status. Open mouth view x-ray were also taken to demonstrate any fracture of the odontoid process. Skull traction was applied in all patients who had C_1 - C_2 dislocation. Cervical x-ray were repeated over days to see how much the subluxation had reduced. A careful watch was kept on their neurological status and it's recovery or deterioration. the smaller group (five cases) of congenital variety. of Atlanto-axial Dislocation were picked up from the out-patient department. These cases had sustained minor trauma to neck and came with complaints of pain neck and decreased range of neck movements. One patient with tuberculosis of C_2-C_3 region came with pain neck after sustaining minor trauma. This group was also managed like the injury group. They were also put in Cervical collar, x-ray were done and cervical traction applied.

Operative Technique

Operation was performed under Endotracheal (flexo-metallic re-enforced), Cervical under General Anaesthesia in prone position. Cervical traction was continued until the posterior fusion was complete. The occiput and the upper cervical spines C_1-C_4 were exposed via a vertical midline incision. Operative technique described here includes features of the procedures used by Cone & Turner, Rogers and Willard and Nicholson. Two drill holes are made in basi occiput, one on either side of mid-line, 2.5 cm superior to the posterior lip of foramen magnum. Drill holes are made at the junction of the base of spinous process where it joins the laminea on either side. Wire is passed through these holes and those in the basi-occiput to give a firm fixation to occipito cervical region under flouroscopic control. Next the split fibular grafts are taken. Drill holes at proximal and distal ends are made in these grafts. The grafts are placed on either side of the spinous processes over the laminae of C_2 & C_3 extending upto the basi-occiput, just fitting snugly in to the basi-occiput at the hole sites. An additional wire length is negotiated through the holes in the basi-occiput and the proximal drill holes of fibular graft and wires tightened. Similar technique is used to fix the distal drill holes of the bone grafts with the base of spinous processes. (Campbell's operative orthopaedics Sixth Edition Page 1974, year (1980). The fixation is undertaken under continuous X-ray control in the operation theatre. The neck muscles of the occipito-cervical region are closed in layers snuggly embracing the graft, the wires and the spinous processes. In our opinion- this wire fixation + bone graft fixation of the occipito cervical region gives a fixation stable enough to prevent displacement of fibular graft. In our earlier cases we have been using Iliac crest as a donor site. These patients are operated in cervical traction and continue to be in traction during their post- operative period. Skeletel traction is reduced to about 5 pounds and is continued during the period of rest in bed. The patients are kept in Bed for a period of three weeks. The patients are given a neck collar before they are allowed to sit up or moblised after three weeks.

Results

There were no operative or immediate post operative complications. Emphasis was given to intra-operative fluoroscopy as the. stablization was being carried out. The wires were fixed in such as way that the neck remained in slight extension in its final position. Complications after surgery are analyzed in Table IV. twenty five patients have had a follow up of more than 15 years. The results of the fusions have been mostly excellent (22 cases) 70.9%. Long term complaints have been minor episodes of positional vertig, shoulder discomfit. Restriction of neck movement and occasional paraesthesias of hands. We have not seen any cause of recurrent dislocation. In one patient the wire snipped off at one end after 5 years of surgery. This was detected on routine follow x-ray of the region. One patient had recurrent trauma to neck. Although the x-ray of the fusion area did not show any radiological abnormality the patient was distresed with vague paraesthesias, burning, etc. She settled down with anti depressant drugs and cervical collar. By and large, most of the operated patients showed improvement in their symptoms.

Table IV: (Atlanto-Axial Dislocation)

Post-operative complaints	
◆ Reduced ROM Neck	29
◆ Shoulder Discomfort	13
◆ Paraesthesias	06
◆ Wound infection	02
◆ Mortality	00

Discussion

Malformation of Atlanto-occipital region have been recognized for many centuries[1]. Cranio Vertebral anomalies are as results of faulty development of the axial skeleton and of the enclosed neuraxis at the Junction of the spine and the cranium. The clinical syndromes associated with these anomalies are attributed to: i) Pressure on the neuraxis by bony abnormality, malformation of the nervous system, and disturbance of CSF circulation and blood supply.

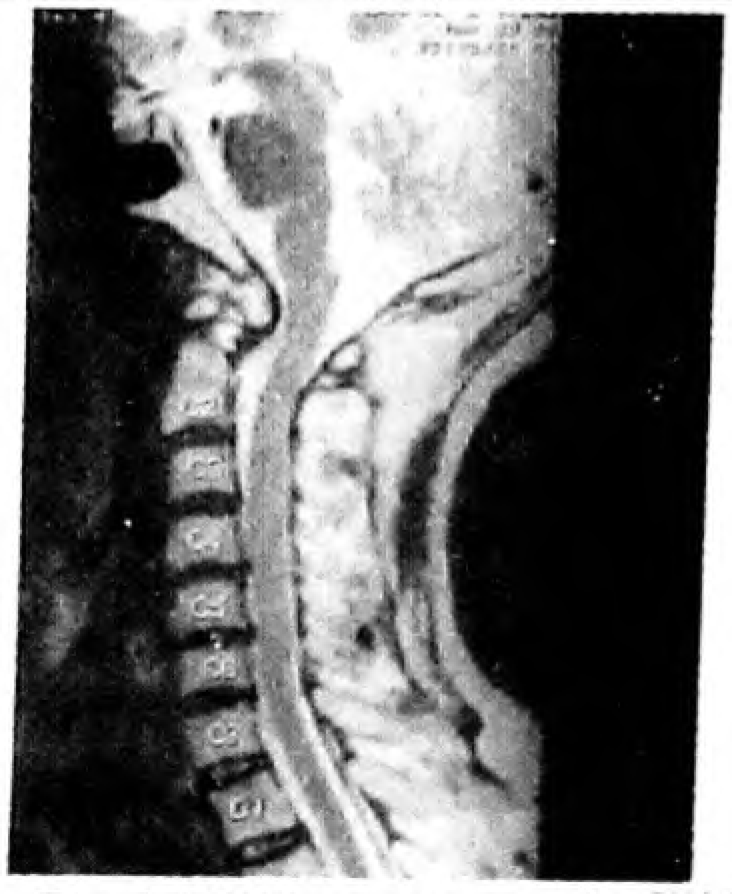


Fig. I. MRI CV Junction showing fracture odontoid process

The mangement of patients with Atlanto-axial instablity remains a complex and challenging problem for the neurosurgeons[2]. Dislocation may result from congenital malformations, trauma, infections, rheumatoid arthritis, subluxations, neoplasm or other degenerative disease processes.

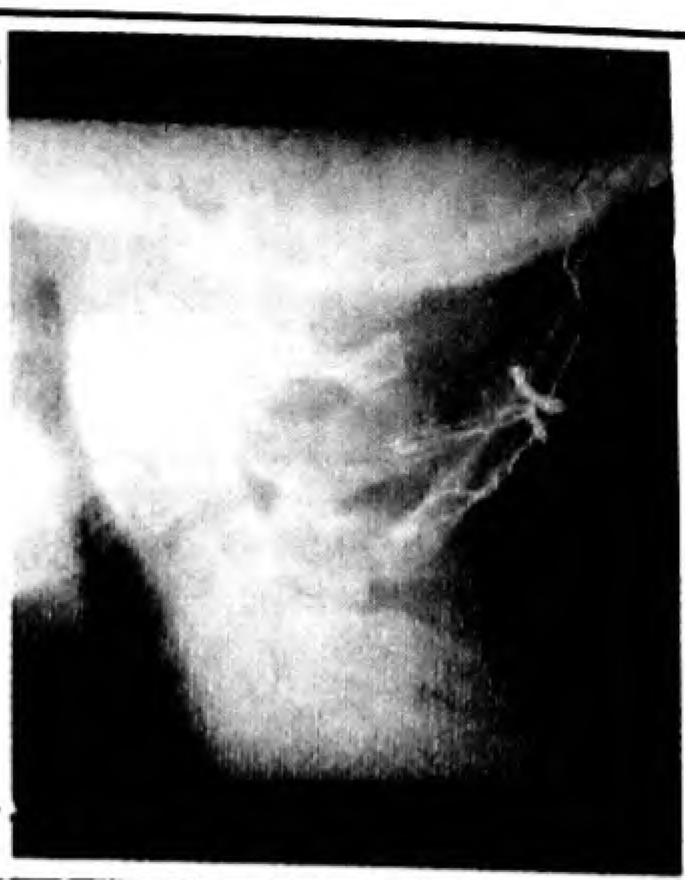


Fig. II. Post operative x-ray showing posterior wiring and fusion with bone graft

In our series, a majority of subluxations (25) were due to trauma. Seven cases had fracture of the odontoid process (Fig-I).

In congenital dislocations minor trauma may occur and aggravate symtoms. The dislocation may occur during childhood[5,6] and patients complain of pain neck later on. In present series our experience has been similar. Pain in the neck with limitation of neck movement was the main complaint in all such cases. Another major complaint was transitory paraesthesias in limbs as well as episodes of giddiness. One of our patients came with progressive neuroloical signs, principally involving the pyramidal tracts and posterior columns. We did not encounter any patient with sleep aponea or Narcolepsy[7]. X-ray of the cervical spine taken in flexion and extension provided maximum information about the morbidity of the affected spine. Tomograms were essential before CT scan era and are still done[1,8]. Magnetic rasonance Imaging (MRI) is an excellent imaging tool for diagnosing these dislocations (Fig.I). CT Scan is also very helpful. In post traumatic dislocation, we observed fracture C_2 in 15(48.3%) cases. the rest 16(15.7%) all showed a mal-aligned axis. Separate odontoid tip was seen in three cases of congenital variety. We did not encounter any case of assimillated atlas or fused vertebral bodies in our group of congenital Atlantoaxial Dislocation. The goal of treatment is aimed at reducing pathologic subluxation, restoring Atlantoaxial stability and to protect spinal cord.

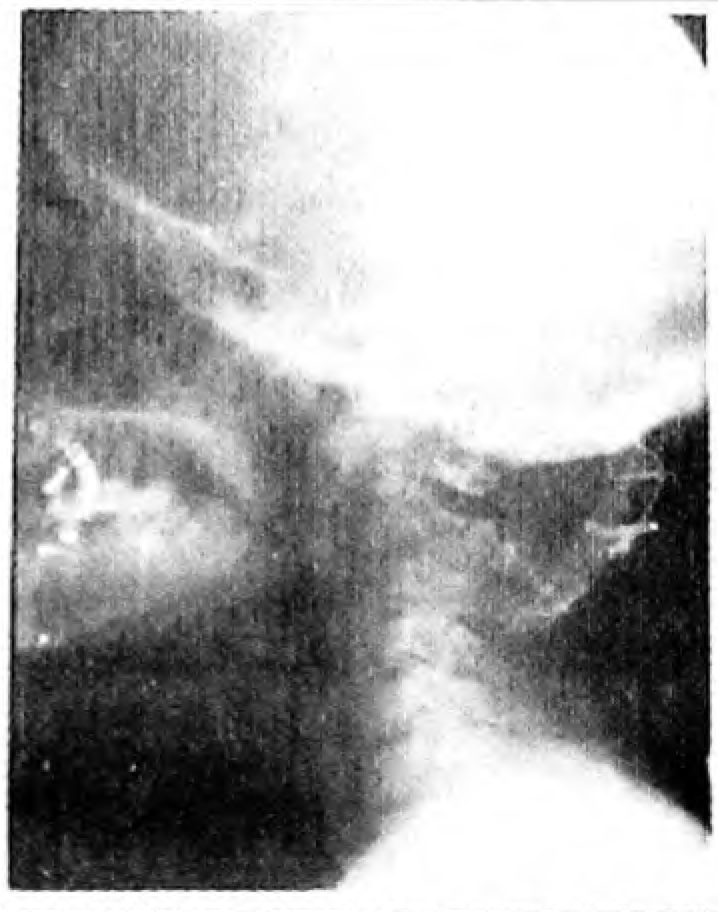


Fig. III. Post operative x-ray showing posterior wiring and fasion with bone graft

Once diagnosis has been confirmed, the most initial step is to put the patients in cervical collar and immediate cervical traction by using skull calipers. The check x-rays are done and neurological status is frequently checked. The weights are increased gradually till the check x-rays show an optimum reduction in the subluxation. Improvement in patients neurological condition[9,10] and alignment of the bones are the best guides to adequate decompression. All patients are operated under endotracheal general anaesthesia while the patient is still in traction. Mixture and so good first described a patient with Atlantoaxial Dislocation successfully treated by fixing the atlas to the spinous process of the axis with a silk thread. Standard posterior mid line approach is used to expose the occiput and upper cervical spine upto C_3.

The graft, in our series, was taken from fibula in a majority of cases. Other authors use graft from Iliac crest[9,10]. We have also used Iliac crest grafts in some of four cases. The patients are moblized after 3 to 4 weeks. During post operative period they have to wear cervical support (Collar). At the end of three months cervical support is worn at intervals. Discontinued during sleep and worn while moving around. The stability of the graft and wire fixation is assessed by taking translateral x-rays of the Atlanto occipital region in mild to moderate flexion/extension. If there is no undue mobility of the odontoid at the atlanto-axial joint, we presume the patient has a stable atlanto—occipital region.

The overall result of surgical management in post Traumatic Atlantoaxial Dislocation have been good to excellent variety, the result of surgery have been similar to the post-traumatic group[9,10,11,12,13]. Once complex and multiple anomalies are associated with the Atlanto-axial Dislocation, the result have not been so encouraging because of the involvement of neuroaxis and the vascular changes in the Neural structures. Results of treatment are also not encouraging in the cases, where patients report to the hospital in an advanced stage of the disease (with myelopathy).

Conclusion

Unique anatomy and biochemical properties of the Atlantoaxial complex make treatment of Atlantoaxial instability a formidable challenge for the Neurosurgeons/ Spinal Surgeons. A large variety of mangement strategies and surgical techniques have been suggested in order to achieve stability of atlanto axial joint. This article is trying to convey the management protocol we follow in managing the Atlantoaxial Dislocation at a regional Neurosurgical centre in India.

References:

1. Sinh G. Cranio Vetrobral Anomalies. 1995; In texts book of Neurosurgery. B. ramamurthi and P.N. Tendon (Eds.): National Book trust, Delhi; pp 199-210.
2. Karaholios D.G.; Apostolides P.J; Sontag V.K.H. Stablization and fusion techniques for Atlantoaxial instability, Crit. Rev. Neurosurgery, 1996;6:13-19.
3. Sontag V.K.H: Dichman C.A. Clin. Neurosurg (1993) 40:243-272.
4. Dickman C.A; Sonntag V.K.H. (1995) In: Schmidek H.H; Sweet W.H. (Eds.) operative Neurosurgical techniques; 3rd, d, Saybders. Philadelphia pp 1849-1873.
5. Wadia N.H. Chronic Porgressive Myelopathy Complicating Atlantoaxial dislocation due to congenital abnormality (1960). Neurology 81-83.
6. Wadia N.H. Myelopathy complicating congenital Atlanto axial Dislocation. A study of 82 cases (1967(. Macmillan (Journals) Ltd. 449.
7. Pandya S.K. Atlantoaxial Disalocation. Review (1972) Neurology India. 20:13-16.
8. Hall CW. Danoff D: (1975) Sleep attacks - apparent relationship to Atlantoaxial dislocation. Surg. Neurol. 32-57.
9. Balasubramaniam V. Ramamurthi B: (1960) Cranio-vertebral anomalies with Neurological symptoms. Ind. J. Surg. 22.119.
10. Singh G: (1975) Atlantoaxial dislocation. Presidential adress. Neurological Society of India. 25th Annual Conference, Chandigarh.
11. Chatterajee RN: (1973) Congenital atlantoaxial islocation. Paper read at the 23rd annual conference of the Neurological scoeity of India Ahmedabad 1973.
12. Gulati DR. Rout D: (1974) Atlantoaxial dislocation with quardipraresis in achondroplasis. J. Neurosurg. 40:395.
13. Jain VK, Takayasu M. Singh S, Chharbra DK. Sugita K (1993) Occipital-axis posterior wiring and fusion for atlantoaxial disloation associated with occipitalization of the atlas. Technical note. J. Neurosurg 79:142-144.
14. Greengerg AD; (1968) Atlantoaxial dislocation. Brain. 91:655.
15. Srinivasan K. Balasubramaniamv. Ramamurthi B: (1967) Craniovertebral anomalies.A study of 24 cases. Neurol. India. 15. 42.
16. Baarros MC. Farias W, Ataide L, Lins S: (1968) Basilar impression and Arnold Chiari malformation. A study of 66 cases. J. Neurol. Neruosurg. Psychiat. 31.596.
17. Driesen W. Oldenkott P. Rossi U: (1966) Operative resultsof basilar impression and related deformities of the Atlantooccipital region. Acts. Neurochir. 15:83.
18. Ramamurthi B, Viswanathan GS: (1957) paget's disease of the axis causingquadriplegia. J. Neurosurg. 14:580.
19. Duong DH. Chadduck WM (1994) reconstruction of the hypoplastic posterior arch of the atlas with calvarial bone graft for posterior atlantoaxial fusion. Technical report. Neurosurgery 35:1168-1179.
20. Gel A. Laheri V (1994) Plate and screw fixation of atlantoaxial subluxation Acta Neruochir (Wien) 129:47-53.
21. Fidler MW. Valentine NW, Rahmatulla AT (1994) Posterior Atlantoaxial fusion; a new internal fixation device. Spine 19: 1397-1401.
22. Subin B. Liu JF. Marchall GJ. Huang HY. Ou JH, Xu GZ Transoral anterior decompression and fusion of chronic irreducible atlantoaxial dislocatin with spinal cord compression (1995). Spine 20:1233-1240.
23. Mcrae DL, Barnum AS; (1953) occipitalisation of the atlas, Amer J. Roentgenol. 70:23.

CLINCO - RADIOLOGICAL PROFILE OF SPINAL CORD TUMORS

Raja Zahid M.S.; Parvez A. Shah D.M.; Sofia Muzzafar M.D.

***Abstract:** The present study comprising of twenty nine cases of compressive myelopathy depicts their clinicoradiological features. Majority of the patients belonged to fourth and fifth decades with equal gender distribution. Thoracic region was involved in 75% cases. Motor weakness, sensory distrurbances and sphincteric dysfunction were observed in 79%, 65% and 55% cases respectively. Extra dural, intradural extramedullary and intramedullary tumors were present in 19, 8 and 2 cases respectively.*

Key words : Spinal cord, tumor.

JK-Practitioner 1999; 694):286-288

Introduction

Spinal tumors are an important cause of cord compression and as such their early diagnosis is of paramount importance in preventing irreparable cord damage. Tumors of the spine whether of neural or extra neural origin have been diagnosed by various imaging modalities like plain X-ray and Myelography and MRI. The parameters that are used for the diagnosis of spinal tumours on plain x-ray include: erosion of a part of the body of verteba, lateral masses or posterior elements and calcification within the tumour. The horizontal distance between vertebral pedicles, when increased on plain x-ray, indicates erosion of pedicles & enlargement of the tumor. However only about one-third of spinal tumors are large enough to produce erosion of vertebra on plain radiographs[1]. To have a better localisation & classification of spinal tumors myelographic finding of "a filling defect" in the dye column is used to differentiate between extradural, intradural extra medullary & intra medullary tumours of spinal cord. Unfortunately myelography has certain draw backs, such as:- 1. It is an invasive procedure, 2. Insufficient quantityof dye may lead to non-visualisationof the spinal tumor, 3. Pseudo-defects may occur such as localised hematoma, prolapsed disc, 4. Deformities of spine such as kypho-scoliosis make it difficult for the dye to move into the upper thoracic and cervical areas. 5. Painful conditions of spine may not allow proper manouvering of patient for the proper distribution of the dye, 6. Anatomical variations of spinal `cul-de-sac' may prevent dye from going into the lumbar and lumbo-sacral areas. A `short cul-de-sac' culminates one or two segments above normal and may change the diagnosis on myelography. A narrow cul-de-sac' may give false picture resembling a spinal tumor, 7. Previous surgery of spine may result in thickened meninges and adhesions which are prone to produce filling defects, and may be wrongly interpreted as spinal tumors on myelography.

Besides myelography & MRI, computerised tomography scan (CT Scan) also constitutes an importantdiagnostic tool for various compressive lesions of spinal cord. In an under developed country like India, facilities for MRI cannot be offered to each & every patient because of its non availability in most of the centres, CT has been found to be useful in the diagnosis of spinal tumours because it is atraumatic, easy to perform and exact contours of tumors can be ascertained. It also helps in displaying relation of tumor to surrounding structures, besides giving exact anatomical level & size of spinal tumors[2]. Contrast enhanced spinal CT has been found to be more effective method for detailed evaluation of spinal tumors[3,4].

Materials and Methods

The present study comprises of29 cases who presented with clinical features compatible with diagnosis of compressive myelopathy. Besides a detailed history, a thorough neurological examination was performed to ascertain the nature of neurodeficit and possible anatomical site of the lesion. The patients were subjected to the following investigations:

a) Plain Radiography
b) Myelo-graphy
c) CT -Myelography. (Contrast Enhanced CT)

From the Department of Orthopaedics (Zahid) Medicine (Shah) and Radiodiagnosis & Imaging, (Sofi) Govt. Medical College, Srinagar, Kmr.

Received March 1999 Accepted July 1999

Correspondence to : Dr. Raja Zahid, 16, Parsi Bagh, Jawahar Nagar, Srinagar, Kashmir, J&K, India.

Contrast (Iohexol) was injected intra-thecally and CT scan was performed 3hours later. Relationship of compressive lesion to spinal Cord, theca, and any assoicated bony abnormalities were carefully looked for.

Attenuation value of various spinal space occupying lesions (spinal tumors) depending upon the type of tissue involved was also determined using Hounsfield units for various types of tissues.

Results

Majority of the patients with compressive myelopathy due to spinal tumors belonged to fourth and fifth decades with almost equal gender distribution (Table-I). Thoracic region was involved in 75% cases (Table-II), Common presenting features such as motor weakness, sensory distrubances and sphinctericdysfunction were noticed in 79%, 65% and 55% cases respectively. Amyotrophy of hand muscles was observed in all the three cases with cervical myelopathy (Table-III).

Table No. 1: Age and Sex distribution of 29 cases of Spinal - Tumors

Age-Group (Year)	No. of Cases	Ses Male	 Female
11-20	3	-	3
21-30	6	4	2
31-40	9	5	4
41-50	5	3	2
51-60	4	1	3
61-70	2	2	-
Total	129	15	14

Table-II: Region of Spinal Cord Involved by Spinal Tumors

	Level	No. of Cases	%age
1.	Cervical	3	10.34
2.	Thoracic	22	75.86
3.	Lumbar	4	13.79
	Total	29	100

Table-III: Spectrum of Clinical Features in 29 cases of Spinal Tumors with Cord Compression

	Parameter	No.of Cases	%age
1.	Motor Weakness	22	75.86
*2.	Sensory Disturbances	19	65.51
**3.	Sphincteric Dysfunction	16	55.17
4.	Upper Motor Neuron Sign	23	79.31
5.	Amyotrophy of hand Muscles	3	10.34

**Includes graded sensory loss, suspended sensory loss.*

*** Includes precipitancy & hesitancy.*

Table No. 4

Myelo-CT Characteristics of 29 cases of Spinal Tumors

Case No.	Level	Anatomical Type of Lesion	Position in Relation to Cord/THECA.	Cord Comp-ssion	Density of Tumour	Involvement of Osseous Vertebra	Associated Findings
1.	2.	3.	4.	5.	6.	7.	8.
1.	C4-C5	ED	Antero-Lat (L)	+	Fluid	-	-
2.	D2-D3	IMED	Indeterminate	+	Soft-Tissue	-	-
3.	D12	ED	Indeterminate	+	Variable	+	-
4.	D10-D12	IDED	Left	+	S.T.	-	-
5.	D7	ED	Antero-Lat(L)	+	Mixed	+	-
6.	D8-D9	ED	Postero Lat(L)	+	S.T.	+	-
7.	D6	ED	Antero-Lat(L)	+	S.T.	-	-
8.	D5,6,7	ED	Circumferential	+	S.T.	-	-
9.	D3,4,5	ED	Right	+	Cystic	-	-
10.	D4-D8	IDED	From Cord Substance	+	Nervous Tissue	+	+
11.	D7-D9	I.M.	Central	+	Nervous Tissue	-	-
12.	D5-D6	IDED	Left	+	Nervous Tissue	-	-
13.	D2-D4	IDED	Anterior	+	S.T.	-	-
14.	D8-D9	ED	Anterior	+	Hemopoietic	+	-
15.	D8-D9	IDED	Anterior-Lat(R)	+	S.T.	-	-
16.	L5	ED	Anterior-Lat(R)	+	S.T.	+	-
17.	D5-6	ED	Postero Lat(L)	+	S.T.	-	+
18.	L3-L4	ED	Posterior	+	BLOOD	-	-
19.	L5	IDED	Postero Lat(L)	+	S.T.	-	-
20.	D4-D7	ED	Posterior-Lat(R)	+	Hemopoietic	-	-

21.	C5-C6	ED	Postero-Lat(L)	+	S.T.	-	-
22.	D5	ED	Anterior-Lat(R)	+	S.T.	-	-
23.	D10	ED	Poterior	+	S.T.	-	-
24.	C7	IDED	Anterior	+	S.T.	-	-
25.	L2	IM	Circumf	+	Blood	-	-
26.	D3	ED	Postero-Lat(L)	+	Blood	-	-
27.	D7	ED	Anterior-lat(L)	+	S.T.	+	-
28.	D4	IDED	Circumf	+	Blood	+	-
29.	D10	ED	Postero-Lat(R)	+	S.T.	+	-

Abbreviations: ST = Soft Tissue, L = Left, R = Right, Circum = Circumfrential.

- The table shows that all of the 29 cases of spinal tumors had compression of the cord.
- 19 cases had extra dural, 8 Intra dural-extra medullary while 2 cases had Intra medullary tumors.
- In 7 patients tumor was Antero Lateral in location while in other 7k it was postero laterally situated.
- 2 patients had central cord tumors.

Beakup of tumors according to density of the tissue revealed tumors originating from soft tissue in 15 cases, nervous tissue in 4 cases, hemopoietic in 3 cases while frank-blood was found in 3 cases. Cystic masses were seen in 2 cases while mixed density tissue was seen in 2 cases.

Discussion:

CT especially with intrethecal contrast precludes many of the errors seen with myelography. In our series of twenty nine patients with compressive myelopathy, a detailed picture of each spinal tumor was possible on CT (Table-IV). Important features like position of tumor in relation to cord, theca, midline, type of tissue comprising the tumor (as shown by CT attenuation value)were all clearly seen. This was of importance while contemplating the surgical approach for the spinal tumor. The tissue comprising the tumor was delienated welland its approximate composition was determined by noting its attention value in Houns field units. Thus CT was able to differenciate between solid, fluid and mixed variety of tissues within the tumor and was helpful in giving a probable diagnosis about the type of tissue involved. It was thus possible to see that the spinal tumors were mostly composed of solid masses comprising soft tissue predominantly of neural or neuro-fibrous origin. CT was able to differenciate between plain fluid and frank blood in-tumor. Thus hemopoietic tumors were picked up clearly. Our results are corroborating well with those of other studies[2,3,4]. All these studies have shown that CT is a superior diagnostic imaging technique for the diagnosis of spinal tumors.

Referebces:

1. Camp, J.D: "The roentgenologic localisation of tumours affecting the spinal cord" Section of roentgenology. The Mayo-Clinic Sep 1938;13-17.
2. Baleriaux - Waha, D., Terwinghe, G, Jeanmart L, "The value of computed tomography for the diagnosis of hour glass tumors of the spine". Neuro - radiology 1977;14:31-32.
3. Resjo M, Harwood - nash C, Fitz C.R.: "CT metrizamide myelography for intra spinal and paraspinl neoplasms in Children" AJR, 1979;132: 367-372.
4. Boheman, H.H., Sachs B.L., Carter J.R., "Primary Neoplasms of cervical spine: Diagnosis and treatment of 23 patients". Jr. Bone & JOint Surgery 1986;68(9):483-93.

JK-PRACTITIONER

ABDOMINAL COMPLICATIONS OF VENTRICULO-PERITONEAL SHUNTS IN CHILDREN

Nasib C. Digray M.S. M.Ch.; Mohit Arora M.B.B.S; Yogeshwar Mengi M.S. M.Ch.;
H.L. Goswamy M.S. M.Ch.; D.R.Thappa M.S.; K.K. Gupta M.S.

***Abstract:** Seven children presenting with various abdominal complications of Ventriculo-Peritoneal (VP) shunts are reported. All patients had complications with in 6 months of their shunt surgery. Two patients each had intestinal obstruction, peritoneal CSF pseudocysts and non-absorbing CSF ascites. In remaining one patient the peritoneal end of the shunt tube prolapsed through the anus after perforating the gut. There were no abdominal signs of perforation but the patient had features of ventriculitis and raised intra-cranial tension (ICT). This interesting case is described in detail under the title "Patients and Methods". Shunt revision and alternative procedures were required in all except two patients with intestinal obstruction and one with CSF pseudocyst.*

***Key words:** Hydrocephalus, Ventriculo-Peritoneal Shunts, Ventriculitis, Bowel Perforation, CSF Pseudocyst.*

JK-Practitioner 1999;6(4):289-291

Introduction

Complications following CSF peritoneal shunts for hydrocephalus are common, requiring multiple revisions/ alternate procedures. though shunt infections and blockabe are commoin after all types of CSF shunts, abdominal complications are not rare after VP shunts. Adhesive intestinal obstruction, CSF pseudocysts and non-absorbing CSF ascites because of low grade peritonitis and/or immune reaction have all been reported. Furthermore, distal shunt tubes may erode any abdominal viscera, especially gut. These patients present with features of acute abdomen and/or ventriculitis. In some cases, the peritoneal catheter after perforating the intestine has prolapsed per anus. We review 7 cases of abdominal complications of VP shunts, including one patient who presented with prolapsed shunt tube through anus.

Patients and Methods

Seven children with abdominal complications of VP shunts seen over a period of 5 years are reported. Congenital hydrocephalus without spina bifida was the primary lesion in all the cases. The age at the time of surgery ranged between 6 months to 2 years. All the complications occurred within 6 months of surgery, the earliest being after 2 months. There were 4 male and 3 female patients. The various complications are depicted in table 1. One patient who had ventriculitis because of intestinal perforation and prolapsed shunt tube per anus is presented as a case summary. The diagnosis of the complications was mainly clinical, however, X-ray abdomen and ultrasonography (Abdomen/Head) was done whenever required. CSF analysis were done in all the cases.

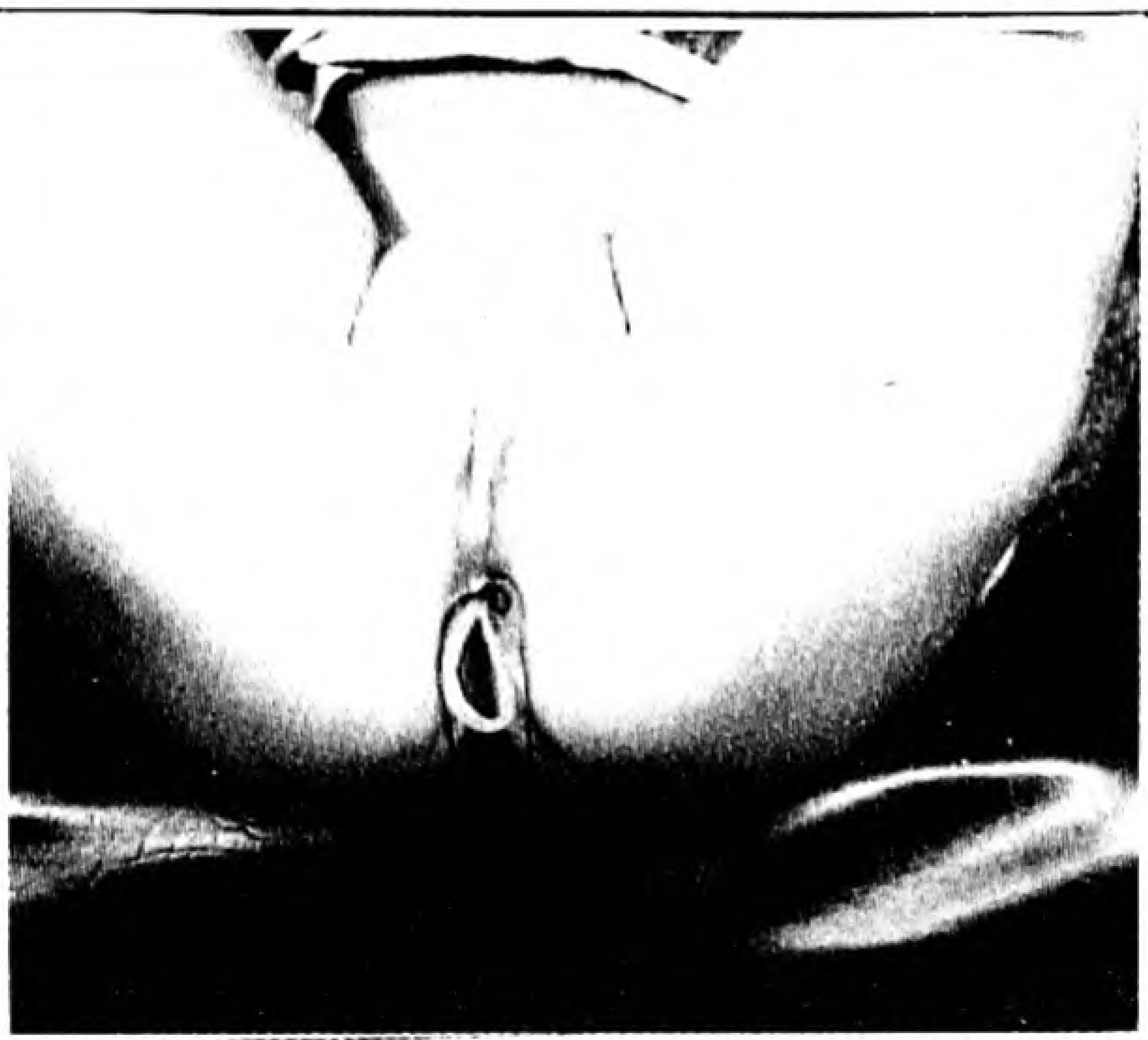


Fig. I Per-anal prolapsed peritoneal catheter of VP shunt in a child. The patient had severe ventriculitis without any clinical/ radiological abdominal signs.

Case Summary

A 2 year old female child presented with vomiting, refusal to take feeds, neck stiffness and irritability for 2 days. The patient had undergone a VP shunt (Uppadya MDR) for congenital hydrocephalus 4 months ago and had been

From the Department of Surgery (Pediatric Division) (Digray, Arora, Mengi, Goswamy, Thappa and Gupta) **GMC, Jammu, J&K State (India)**

Received September 1998 Accepted June 1999

Correspondence to : Nasib C. Digray, 220-Sarwal Colony, Jammu, J&K-India 180 005. Fax: 0091-547647

Table-I: Abdominal complications of VP shunts (n=7)

Complications	No. of Cases	Cause	Treatment	Outcome
Intestinal obstruction	2	Adhesions between Omentum & gut loops	Laparotomy & adhesionolysis	Recovered, Patent Shunts in both pts.
Shunt Malfunction	2	Non-absorbing CSF Ascites	Alternate sunts VA=1, VC=1	Recovered, shunts functioning.
Blocked shunts	2	Peritoneal CSF pseudocyst & omental plugging of tube	Exicision of pseudocyst & shunt revision.	Shunt revision needed in 1 case.
Ventriculitis & shunt prolapse per anus	1	Bowel perforation	Removal of shunt Ext. ventriculostomy Antibiotics	Recovered, shunt revised.

VA= Ventriculo-atrial, VC= Ventrculo-cholecystic

seen in follow up clinic 3 weeks prior to the onset of the present symptoms. One day after the onset of the symptoms the parents noticed the protrusion of the shunt through the anus after defecation. They, however, denied any abdominal complaints by the child. A private practitioner who saw the child, ligated the tube when he noticed the clear fluid dripping through the protruding tip of the tube. This however led to deterioration in the condition of the child. On examination the child was febrile with mild dehydration. The anterior fontenella was full and tense. Neck stiffness was present with brisk tendon reflexes but without any focal neurodeficit. Abdominal examination was normal. The peritoneal end of the shunt tube was seen coming through the anus with a tie over it (fig.1). On digital rectal examination, the catheter was freely mobile in the rectum and its entry point appeared to be high up beyond the reach of the finger. Investigations revealed a marked polymorphonuclear leucocytosis. Blood culture was sterile. Abdominal x-ray and ultrasound (US) did not show any evidence of peritonitis/ pnemoperitoneum. Cranial ultrasound revealed hydrocephalus with severe ventriculitis. CT scan of the head was not done. CSF biochemistry and culture studies showed exudative ventriculitis because of mixed coliform organisms with predominance of Esch. Coli. The patient was put on IV Ceftriaxone and IV fluids. The distal catheter was removed by pulling the protruding end through the anus and the ventricular catheter through an incision over the scalp. An external ventriculostomy was made by inserting new ventricular catheter and shunt chamber. Repeated CSF analyses were done till they were near normal when a revision of the shunt was caried out. The patient is doing well 3 months postoperatively.

Results

The outcome of the results following various procedures for abdominal complications of VP shunts are summarized in table 1. Both the patients who had intestinal obstruction, adhesions were found between the gut loops, omentum and the right lobe of the liver. In one patient part of the omentum was acting as a band compressing the small bowel. Adhesiolysis was done to relieve the obstruction, however, the shunts were patent in both the patients. In two patients who had peritoneal CSF pseudocysts diagnosed on ultrasonography, the distal shunt end was found obstructed by the omentum with a localized collection of CSF. The pseudocysts were excised/deroofed and the shunt tube was placed over the right lobe of the liver. In one patient the revised shunt worked well while in the other it had to be converted into VA shunt for re-obstruction by the pseudocyst. Two patients who had non-absrobing ascites, the shunts were found to be patent. However, these were revised to VA and VC shunts. CSF studies and peritoneal biopsies inpatients of pseudocysts and that of non-absorbing CSF ascites were normal. All 17 patients after a follow-up of 2 months to 4.5 year are doing well with patent shunts and no abdominal problems.

Discussion:

Complications following VP shunts occur in many patients with shunt infections and blockage leading the list. It has been seen that more than half of the shunted hydrocephalic patients may require revisions/alternate procedures for these complications[1]. Abdominal complications of VP shunts, though, occasionally reported are not uncommon and at times may be life threatening due to gram negative infections[2]. Some patients may present with features of acute abdomen because of gut perforation, peritonitis and intestinal obstruction[3-5], while others have malfunctioning/blocked shunt because of tense ascites and abdominal pseudocysts[6,7]. Whereas the etiology of intestinal obstruction and perforation following VP shunts is obvious, other complications, like non-absorbing ascites and abdominal pseudocysts are mainly because of subclinical peritoneal infection and in some cases due to an immune reaction[6]. These patients usually present with malfunctioning shunts and are best diagnosed by US. Patients who have gut perforation due to VP shunt present with peritonitis, ventriculitis or both. A review of 12 such cases by Schulhof et al[3] revealed that clinical peritonitis was initially present in two patients but subsequently developed in 4 others. Five of these patients had Gram negative ventriculitis. In 7 patients the shunt tube had protruded through the anus as in one of our cases. It is not uncommon for a patient with infected VP shunt to present as acute abdomen. In a series of 19 such patients, Reynolds et al[5] found that all had peritonitis without any intestinal perforation. Three children who underwent surgery with pre-operative diagnosis of acute appendicitis were found to have infected shunts and peritonitis with no other pathology. All the patients settled on conservative treatment with IV fluids, antibiotics and external ventricular drainage. Similar cases have, also, been encountered by other repoters causing delay in diagnosis and unneccessary surgical interventions[8,9].

CSF pseudocysts may form in 4-5% of cases with VP shunts, presenting as shunt obstruction, abdominal pain, lump or intestinal obstruction[7,12]. Presence of pseudocyst is highly suggestive of infection in any patient with VP shunt. An active infection is present in 30%, while a recent history of shunt infection may be elicited in 62% of these cases. Other workers have shown a figure of 80% with pseudocyst having shunt infection[11]. However, despite best efforts peritoneal infection could not be established in any of our patients with pseudocysts.

In summary we can say that[1] VP shunts are commonly associated with infection and blockage, however, abdominal complications are not rare[2]. Shunt infections may present as acute peritonitis and conservative treatment along with external ventriculostomy is effective treatment[3]. Abdominal pseudocysts and non-absorbing ascites are mostly because of shunt infection, requiring revision/alternate shunt procedures in most of the patients[4]. Perioperative use of antibiotics has convincingly reduced the infective complications and is routinely recommended[5]. Gut perforation with shunt tube may present as acute abdomen and/or ventriculitis. In some of these cases the bowel perforation may remain silent, but it is not unusual to find the shunt tube prolapsed through the anus[6]. Intestinal oobstruction occurring due to the shunt tube does necessarily mean that the shunt is blocked.

Acknowledgments

The authors are highly thankful to M/s Eli-Lilly Ranbaxy Ltd. (MEdical information series) for their help in providing the literature in the preparation of this article.

References:

1. Borgbjerg BM, Gjerris F, Abheck MJ et al. (1995): Frequency and causes of shunt revisions in different cerebro-spinal fluid shunt types. Acta Neurochirur. 136(3-4): 189-94.
2. Sells CJ, Schurtleff DB, Loesser JD91977): Gram -ve CSF shunt associated infections.Pediatrics. 59:614-618.
3. Schulhof LA, Worth RM, Kalsbeck JE. (1975): Bowel perforations due to peritoneal shunt. Surgical Neurol. 3:265-268.
4. Murtagh FR, Quencer RM, Poole CA. (1980) Extra-cranial complications of cerebro-spinal fluid shunt function in childhood hydrocephalus. AJR. 135(4): 763-766.
5. Reynolds M, Sherman JO, Mclone DG. (1983): VP shunt infection masquerading as an acute surgical abdomen. J. Pediatr. Surg. 18:951-953.
6. Blount JP, Haines SJ (1966): Infections of cerebro-spinal fluid shunts. In Youman's Neurological Surgery, 4th Edition, Vol.4, pp945-966.
7. Rainov N, Schobess A, Heidecke V et al. (1994): Abdominal CSF pseudocysts in patients wih ventriculo-peritoneal shunts. Acta.Neurochirur. 127(1-2);73-78.
8. Rubin RC, Ghatak NR, Visudhipan P. (1972): Asymptomatic perforated viscus and Gram-ventriculitis as a complication of a valve regulated VP shunt. J. Neurosurg. 37:616-619.
9. Hubschmann JR, Countee RW. (1980): Acute abdomen in children with infected VP shunts. Arch. Surg. 115(3): 305-307.
10. Hahn YS, Engelhard H, Mclone D. (1985): Abdominal CSF pseudocyst: Clinical features and surgical management Pediatr. Neurosci. 12:75-79.
11. Gaskill SJ, Martin LE. (1989): Pseudocyst of abdomen associated with infected ventriculoperitoneal shunts, Pediatr. Neurosci. 15:23-27.
12. Rehman NU, Jamjoom A, Jamjoom ZA. (1996): Intestinal obstruction caused by extraperitoneal cerebro-spinal fluid collection. Pediatr. Neurosourg. 25(3):160-162.

PRIMARY DUODENAL LYMPHOMA - A SHORT STUDY OF SIX CASES

Sheikh Aejaz Aziz, M.D., D.M.; Shoukat H. Khan M.D.; Mushtaq Ahmad M.D.; Azra Shah M.D.; Parveen Shah M.D.; Gul Mohammad Bhat M.D.; Javid Rasool M.D.

***Abstract:** Six patients of primary duodenal Non Hodgkins lymphoma (NHL) were studied retrospectively over a period of 10 years from 1984. The patients mostly presented with nonspecific symptoms of abdominal disease. A non tender upper abdominal mass was the only positive physical finding on clinical examination. An upper gastrointestinal endoscopy revealed gross abnormalities in most of the patients. However the diagnosis of primary duodenal lymphoma was confirmed after a tissue biopsy taken at laparotomy. Four patients had stage IIE (Ann Arbor) disease of diffuse large cell histology. The patients were subsequently managed by a combined modality of combination chemotherapy and abdominal irradiation. At 30 months follow up 4 patients were alive with no evidence of disease.*

***Key words:** Duodenum; Lymphoma; Non-Hodgkin's Lymphoma; Chemotherapy; Irradiation*

JK-Practitioner 1999; 6(4):292-295

Introduction

The heterogeneity in the phenotypic expression of Non-Hodgkins lymphomas with remarkable differences in the clinical features, prognosis and response to treatment is known. The relative immunity of small bowel to tumours is intriguing and enigmatous despite the fact that 3/4th of gastrointestinal tract length and 90% mucosal absorptive surface is comprised by the small intestine, they are least common in duodenum[9]. In this paper, we report our experience with 6 cases of primary duodenal lymphoma.

Case I

A 25 year old male presented with complaints of haemetemesis and malaena. Clinical examination revealed an ill-defined, firm, non-tender mass in the right hypochondrium. The laboratory profile revealed a haemoglobin of 7.6gms% with hypochromic microcytic PBF. Total differential leucocytic counts along with platelets were normal. Liver and kidney function tests were within normal limits. The chest x-ray was normal. Serum LDH level was 712IU/lit. Abdominal USG showed an echogenic mass in the vicinity of right lobe of liver with para-aortic lymph node enlargement. Barium study revealed increased nodularity in the duodenum. The CT of the abdomen revealed a lobulated mass in the upper abdomen adjacent to the para-aortic region displacing loops of intestine. The bone marrow aspirate did nor reveal any abnormality. An upper G.I. endoscopy revealed multiple large ulcers in the first part of the duodenum. Histopathological examination of the endoscopic-biopsy specimen was reported as chronic duodenitis. A diagnostic laparotomy done subsequently revealed a nodular mass in the region of first-part of the duodenum, almost obstructing it. There was enlargement of the infraduodenal and para-aortic lymph nodes. An anterior gastrojujenostomy was performed. Histopathological review of the biopsy from the mass the lymph nodes revealed Non-Hodgkin's lymphoma (NHL), of diffuse small lymphcytic sub-type. Patient was put on combination chemotherapy CHOP (inj. cyclophosphamide IV 75-mg/m^2 day 1, Inj. Adriamycin IV 50 mg/m^2 day 1, Inj. Vincristine IV 1.4 mg/m^2 day 1, Tab. Prednosone P.O 60mg/m^2 day 1 to 5)[11], to be repeated on day 28. Patient received such 4 cycles, followed by 45 Gy external beam radiotherapy to abdomen in 20 fractions at 5 fractions per week. This was followed by 2 more cycles of CHOP. The patient is in complete clinical remission.

Case II

Twenty three years young male presented with a 3 months history of weight loss of 6 kgs, loose motions and abdominal cramps. Clinical examination was normal except severe emaciation with a total body weight of 42 kgs. The laboratory profile revealed a Hb 11.4gm%. Liver function test (total. proteins 5.8 gm, albumin 3.5gm). Serum LDH were 904 IU/l. Kidney function

From the Department of Medical Oncology (Aziz, Khan, Ahmad, Bhat, Rasool) **and Pathology** (Shah, Shah) **SKIMS, Soura (India)**

Received March 1999 Accepted June 1999

Correspondence to : Dr. Shiekh Aejaz Aziz, DM, Asstt. Prof. Deptt. of Medical Oncology, SKIMS, Soura, Post Bag No. 27, Srinagar 190 011, Kashmir (India) Phones : 452029 Ext. 265, 413; Fax : 091-194-473470

test was normal. X-ray chest PA view and a plain x-ray abdomen did not reveal any abnormality. GI barium series revealed mucosal thickening in the duodenum. An upper G.I. endoscopy showed multiple polypoidal lesions in the duodenum. The endoscopic biopsy was reported as NHL, diffuse large cell type. Bone marrow and peripheral blood smear was reported normal. The patient was put on CHOP combination chemotherapy. An endoscopic remission was documented upon completion of four cycles of chemotherapy. This was followed by external beam radiotherapy to abdomen (45Gy/20 fraction/5 fraction per week). Two further cycles of similar chemotherapy were administered. The patient is on regular follow up and is in remission for the last 30 months.

Case III

A thirty year's young male presented with sudden onset of pain in the abdomen and vomiting. He was admitted with a clinical diagnosis of an acute abdomen. The physical examination revealed an ill-looking patient with a pulse rate of 115/minute. Abdominal examination revealed diffuse tenderness. Laboratory investigations revealed a TLC of 16000 per cumm with 95% poly's with normal LDH levels. A plain x-ray chest (PA) and abdomen revealed gas under the right dome of diapharagm. The patient was subjected to laparotomy, showing a nodular mass engulfing the second part of duodenum, with areas of minute haemorrhage. No distinct perforation was visible in the rest of the duodenum, ileum, jejunum or stomach. A biopsy was taken from the duodenal mass and a palliative anterior-gastrojejenostomy was also performed. Histopathological examination of the biopsy was reported as diffuse large-cell lymphoma of duodenum. The patient developed anastamotic-leak and septicaemia on the 5th post-operative day. He later went into renal failure and died on 10th post operative day, however no tumor lysis syndrome was observed during the post operative period.

Case IV

A 40 year old male presented with a 5 months history of nausea, vomiting, pain abdomen and a mass in the upper abdomen. Clinical examination revealed an ill defined mass in the epigastrium. The mass was relatively fixed, non tender and of firm consistency. The laboratory investigations revealed a normal haemogram. Liver and kidney functions were within normal limits. Serum LDH levels were 540 IU/l. X-ray chest PA was normal. Abdominal USG revealed a mass in the para-aortic region with mixed echo pattern. G.I. barium series revealed an intraluminal mass in the duodenum with ulcerations. Endoscopic biopsy was inconclusive. Bone marrow aspirate was normal. At laparatomy an irregular mass in the region of proximal duodenum with enlarged mesentric nodes was found. The mass was fixed and firm in consistency. Liver and spleen were grossly normal. A biopsy from the duodenal mass and adjoining lymph nodes was taken followed by anterior gastrojejunastomy. Histopathology of the biopsy material was reported as diffuse large cell NHL. The patient was subsequently put on 4 cycles of CHOP protocol, and also received 45 Gy's of external beam abdominal irradiation on Cobalt 60, followed by 2 more cycles of CHOP. For last 2 years the patient is in complete clinical, radiological and endoscopic remission.

Case V

A 17 year young male presented with complaints of pain upper abdomen and fever of 15 days duration. Clinical examination revealed an irregular firm mass in the right hypochondrium. Laboratory parameters revealed normal haemogram, liver and kidney functions. Serum LDH levels were 554IU/lt. X-ray chest was within normal limits, and abdominal USG revealed a hypoechoeic mass in the right hypochondrium with minimal ascitis. G.I. endoscopy revealed a nodular thickening in the second part of the duodenum. Endoscopic biopsy was reported as pooly differentiated round cell tumour. Bone marrow examination was normal. At laparotomy the duodenum was found to be thickened, with lymph node enlargement in the sub-pyloric and coeliac regions. Lymph node biopsy was done. On histopathological examination the lesion was reported to be diffuse large cell, Non-Hodgkin's lymphoma. The patient was subsequently put on combination chemotherapy, CHOP regimen. Patient attained clinical remission (confirmed endoscopically) after 4 cycles of such chemotherapy. This was followed by 45 Gy external beam radiotherapy to whole abdomen and additional 2 cycles of chemotherapy. Patient is on regular follow up for the last 1 year and till date there is no evidence of disease.

Case VI

A 25 year young male presented with weight loss, abdominal pain and swelling in the upper abdomen of 2 months duration. Clinical examination revealed an ill defined, non-tender, firm mass in the epigastrium. In laboratory investigation the haemogram, liver and kidney function tests including serum LDH levels were normal. X-ray chest, plain x-ray abdomen were non-contributing. An abdominal USG revealed mass in the upper abdomen with a mixed-echo pattern. There was significant enlargement of coeliac and mesenteric lymphnodes. Upper G.I. endoscopy revealed mucosal hypertrophy in duodenum with irregular ulceration. The endoscopic biopsy was reported as chronic non-specific duodenitis. At diagnostic laparotomy, a nodular mass involving the distal duodenum was found. Coeliac, subpyloric and mesenteric lymph nodes were found to be enlarged. Biopsy from the mass and lymph nodes were reported as diffuse NHL of mixed cellularity. Patient was subsequently put on combination chemotherapy, CHOP regimen and it was also decided to give external beam radiotherapy for a dose of 40 Gy. The patient after completing 4th cycles of chemotherapy did not attend the hospital. Though patient improved symptomatically, a proper evaluation for response could not be done.

Discussion

A primary GI lymphoma is defined as one confined to the G.I. tract and immediate adjacent lymphnodes at the time of diagnosis. Several modifications to make the diagnosis of primary GIT lymphoma have been suggested like absence of palpable lymphadenopathy, absence of mediastinal adenopathy on radiographic evaluation, absence of hepatic or splenic involvement except via direct extension from primary small bowel involvement, normal peripheral blood smear and bone marrow examination (Dawson et al[2]).

The gastrointestinal tract is the most common site of primary extra nodal lymphomas, accounting for 29.5 to 36.7% of all extra nodal lymphomas[1]. In the western population stomach is the most common site, followed by small bowel[5,6]. This is in contrast to the rest of the developing world particularly the middle eastern region where small bowel constitutes the major site for primary gastrointestinal lymphomas[6,7,8].

Small intestinal lymphomas (SIL) are broadly classified into two types based on their occurrence in geographically distinct areas and with a different clinicopathological profile. Classical SIL often referred to as 'western lymphoma' presents with localized tumors mostly in the ileum. Microscopically it has follicles with centrocyte like cells and plasma cells. The other type of SIL found mostly in middle eastern region is called Mediterranean lymphoma or IPSID (immunoproliferative small intestinal disease) or the alpha chain disease. It is characterized by diffuse involvement in the longer segments of small bowel mainly duodenum and jejunum. There is a dense mucosal infiltrate or plasmacytic or lymphoid cells ranging from low to high grade malignancy[8]. Various malabsorptive conditions like Crohn's disease and coeliac disease have been found to predispose SIL. The incidence of SIL is found to be more in patients with congenital or acquired immunodeficiency syndrome.

Duodenum is the least common site of involvement in the western type of SIL, whereas in the Mediterranean type the frequency of duodenal involvement is next only to jejunum[9].

In the study under review, the majority of the patients were relatively of younger age, (Third decade) and predominantly of male sex (5 males, 1 female). Pain in the upper abdomen and palpable mass in the abdomen were the commonest symptoms. The mean duration of symptoms was 2 to 3 months prior to histopathological diagnosis. All the patients were subjected to barium studies revealing abnormalities like an intraluminal mass, nodular thickenings, ulcerations and mucosal thickening. An upper G.I. endoscopy and biopsy revealed duodenal abnormalities which subsequently were confirmed to be lymphoma's in all except one patient which was reported as chronic duodenitis. Laparotomy was done in 5 patients with an intention of knowing the extent of disease, resectability and stage. Tissue and lymph node biopsy at laparotomy taken confirmed the hisoptahtological findings at endoscopy. These five cases subjected to laparotomy were clinically and pathologically staged as II (Ann Arbor). An updated Blackledge staging system could not be used due to paucity of pathological details. Histopathological examination of the cases under review revealed intermediate grade, diffuse large cell NHL in 4 cases and diffuse mixed type of NHL in one case. A single case of low grade diffuse small lymphocytic type of NHL was reported.

The clinical and pathological features of the cases under review correlate with the western type of small intestinal lymphomas. Following surgery one patient died in post operative period. The remaining 5 patients were put on 4 cycles of intensive combination chemotherapy (CHOP). Subsequently these patients were subjected to external beam irradiation of abdomen on cobalt-60. A total dose of 45 Gys in 4 weeks at a rate of 5 fractions per week through AP-PA portals was given and 2 additional cycles of chemotherapy (consolidation) were administered. All these patients achieved a clinical remission by the 3rd/4th cycles of chemotherapy. One patient has been lost to follow-up after achieving remission in the 4th cycle of chemotherapy. 4 patients are on regular follow up for last 2 years and there has been no evidence of disease till date as is confirmed by clinical and endoscopic procedures.

References:

1. Anil K . Gastrointestinal lymphoma and AIDs - related

GI cancer. Gastrointestinal Cancer: Biology, diagnosis and therapy (Lippin-Raven Publishers, Philadelphia 1995).

2. Dawson IMD, Crones JS, Morson BC. Primary malignant lymphoid tumors of the intestinal tract: Report of 37 cases with study of factors influencing prognosis. Br J Surg 1961;49:80-89.
3. Pavyani S, Hoppe RT, Burke JS, et al. extralymphatic involvement in diffuse Non-Hidgkin's lymphoma. J Clin Oncol 1983:1:682-688.
4. Brigette Dragosics, Peter Banre, Thaddans Radaskienicz. Primary gastrointestinal Non-Hodgkins lymphomas. Cancer 1985;55:1060-73.
5. Frances A. Shephered, William K. Evans, George Kutas, Jonathan C. Yau, Paul Dang J Gerald Scott et al. Chemopptherapy following surgery for IE, and IE Non-Hodkgins lymphomas of gastrointestinal tract. Journal of Clinical Oncology 1988;6:253-60.
6. Brandtzaeg P, Halstensen TS, Kett K, Kvajoi P, Dvale D, Rogaum TO, Scott H, Sollid LM. Immunobiology and immunopathology of gut mucosa. Humoral immunity and intraepithelial lymphocytes. Gastroenterology 1989;97:1562-1574.
7. Azab MB, Henry-Amar M, Rougyier et al. Prognostic factors in primary gastrintestinal Non-Hodgkins lymphoma. Cancer 1989;64:1208-1217.
8. Tondini C, Giardini R, Bozzeetti F, Valagussa P, Swantoro A, Bertullir, et al. Combined modality treatment for primary gastrointestinal non-Hodgkins lymphoma: The Milan Cancer Institute experience. Anna Oncol 1993;4:831-837.
9. Shadid MJ, Alami SY, Naseer VH, Balikian JB, Salem AA. Primary intestiknal lymphoma with paraproteinaemia. Cancer 1975;35:848-858.
10. Haber DA, Mayer RJ. Primary gastrointestinal lymphoma. Semin Oncol 1988;15:154.
11. Mckelvey EM, Gottlieb JA, Wilson HE et al. Hydroydanuomycin (adrimaycin) combinationchemotherapy in malignatn lymphoma. Cancer 1976;28:1484.
12. Ontreary K, Nance FC, Becker WF. Primary lymphom a of gastrointestinal tract. Ann Surg 1980;911:593-598.
13. Cooper BT, Read AE. Small intestinal lymphoma. World J Surg 1985;9:930-937.

With Best Compliments From

SUPREME SYNDICATE

Complete Hospital and Laboratory Furnishers and
Pharmaceutical Distributors

267, NURSING GARH, SRINAGAR-190 001 (KASHMIR) PHONES · 471528, 478712; FAX · 0194-430645

AUTHORISED STOCKISTS FOR:

CHEMICALS:
E.Merck (I) Ltd.
B.D.H. Chemicls
S.D.Fine Chem. Ltd.
Hi-Media Laboratories

GLASS WARE:
Durani (German) Glass Ware
Blue Star Glass Slides & Cover Slips

EQUIPMENTS:
Getner Microscopes
Suvira Audio Visual Equipments
Sipcon Microtones/Tissue Processors
Jindal Lab. Equipments

SICKLE CELL DISEASE IN CHILDHOOD

Ghulam Nabi M.D.

Abstract: *In a retrospective study sixty two children (>28 days <12 years) with sickle cell disease (S.C.D.) were admitted in civil hospital Khamis Mushayat from Muharam 1410 up to Dhulhijja 1413 Hijra (H). The diagnosis was based on the history physical examination and the laboratory tests.*

Majority of the patients were between 5-12 years of age (54.83%). Most of the patients were from Gizan (neighbouring low land area at sea level. Southern region of Saudi Arabia). Both sexes were equally affected. Main symptoms were pain in the abdomen and limbs in forty seven patients (75.80%) and fever in thirty seven patients (59.67%). Family history of S.C.D. was positive in thirty five patients (56.45%). Forty four patients (70.96%) had recurrent admissions. Blood transfusion was given in thirty four patients (54.83%). Main clinical signs were pallor in fifty seven (1.93%), jaundice in thirty five (56.45%), undernutrition in twenty three (37.09%), hepatosplenomegaly in twenty (32.25%) and splenomegaly in eight patients (12.90%). Sixty patients were anemic (96.77%). Increased leucocyte count was observed in fifty two patients (83.87%). Main reason for admission was Vaso.occlusive crisis (V.O.C.) and anemia. None of the patient died. It would appear that this disease is one of the cause of morbidity in Southern region of Saudi Arabia.

Key words: *Sickle cell disease; Mediterranean region; Hepatosplenomegaly.*

JK-Practitioner 1999;6(4):296-298

Introduction

Sickle cell anemia was first reported in 1910. Approximately 4% of the worlds population carry a gene for this clinically important disorder. The gene for HbS occurs most commonly in Africa and in areas of African disaspora, principally in the Caribbean and the Americans. It also occurs in localized areas of India, in the Middle East and around the Mediterranean[1]. Sickle cell anemia is widely dispersed throughout Saudi Arabia and other Middle eastern countries. In Saudi Arabia sickle cell gene was discovered by Lehmann and co-workers in 1963[2]. Gene frequency of HbS in different regions of Saudi Arabia is as follows:- Qateef (Eastern region): 0.170; Gizan (Southern region): 0.103; Mecca (Western region): 0.025; Alula (Northern region): 0.081; reported by El Hazmi[2]. Sickle cell disease has been reported from various parts of Saudi Arabia, but it has not been fully explored from high altitude area like Khamis Mushyat. The aim of this study is to find the clinical presentation and the outcome.

Material and Methods

Case records of sixty two patients admitted from 1410 to 1413 H, in Civil Hospital Khamis Mushayt (located in South West region of Saudi Arabia, at the height of 3000 meters from the sea level) were reviewed. The patients were mostly from Gizan and surrounding areas of Khamis Mushayt. The main criteria for inclusion in this study was Sickle cell disease patients with complications like severe anemia, V.O.C. and infection. The follow up data was recorded from the patients: age, sex, residence, nationality, duration of illness, main complaints, clinical signs and complications.

Investigation:- Hemoglobin, total leucocyte count, differential leucocyte count, platelet count, blood group and Rh., sickle cell test, hemoglobin electrophoresis, reticulocyte count, peripheral blood film, Glucose 6 phosphate dehydrogenase test, X-ray chest & abdomen, ultrasonography, electrocardiography, computerized tomography (C.T.) scanning, magnetic resonance imaging (M.R.I.). Patients with clinical features of S.C.D. who had Hb. less than 7 gm% with clinical signs and symptoms were given blood transfusion. Hb. electrophoresis revealed that two of our patients had Thalassemia and were not included in this study. None of our patient had G6PD test positive.

Results

Commonest age group affected was 5-7 years. The youngest and highest age group in our study was 7

From the Department of Paediatrics and Neonatology, Maternity and Children Hospital, Madina Al Munawarah Saudi Arabia (Nabi)

Received February 1999 Accepted June 1999

Correspondence to : Dr. Ghulam Nabi, P.O. Box 6313, Madina Al Munawarah, Saudi Arabia, Telefax (Home) 04-8473170

months & 12 years respectively. Both sexes were equally affected. Sixty patients were Saudis. Forty four patients (70.96%) had recurrent admission. Clinical features are summarized in table I. V.O.C. & anemia was present in majority of the patients. Twenty three patients (37.0%) were undernourished. Increased leucocyte count was observed in fifty two (83.87%) patients. Ultrasonography was done in all the patients & gall stone was detected in 7 years old male child who developed acute chlecystitis & recovered after receiving the treatment. One of the patient, 5 years old male developed hemiplegia on the left side of the body due too cerebrovascular accident (thrombosis), with right side facial nerve palsy (upper motor neuron). Site of the lesion was detected in the brain by M.R.I. Although C.T. scan was done earlier but it failed to detect the site of the lesion. The patient still has left hemiparesis as observed in the follow up clinic. One patient was admitted with sequestration crisis & responded to the symptomatic treatment. Two patients had bone involvement; one had osteomyelitis of the mandible & other had osteomyelitis of the left tibia. Both recovered after receiving the treatment. More patients got admitted during the winter months (Rajab, Shaban, Ramadan & Shawal). Average hospital stay was 5 days. All the patients who came from Gizen were admitted mainly for V.O.C. crisis. For follow up less than 40% patients turned up.

Table I

Clinical Features	Number of patients	Percentage
1. Pain in abdomen & limbs.	47	75.80
2. Fever	37	59.67
3. Pallor	57	91.93
4. Vomiting	13	20.96
5. Giddiness	12	19.35
6. Yellow Coloration of eyes	8	12.90
7. Jaundice	35	56.45
8. Fever	17	27.41
9. Undernourished	23	37.09
10. Hepatosplenomegaly	20	32.25
11. Splenomegaly	8	12.90

Discussion

Sickle cell disease is a global problem with variable distribution. Outcome of this study has shown that sickle cell disease is one of the causes of morbidity in the Southern region of Saudi Arabia in pediatric age group.

Frequent cause of admission in these patients are the complication like V.O.C., Anemia and infection, forty four of our patients (70.96%) had rercurrent admissions. The molecular abnormality occurs in the B globulin chain of hemoglobin in which glutamic acid at position six is replaced by valine[3]. Sickled red cell becomes trapped in the small blood vessel impairing circulation and causing damage to many organs often resulting in sickle cell crisis[4]. Clinically the disease is more severe in this part of Saudi Arabia[5,6,7]. Several modifying factors have been proposed as indicators for the severity and frequency of V.O.C. episodes, these include Hb. F level, Thalassemia, hoplotypes, RBC deformit[7]. Besides V.O.C., Anemia and infection which were the main reasons for admission of these patients, other clinical features in this study were musculoskeletal pain, pyrexia, pallor, jaundice, hepatosplenomegaly. Similar observations were reported by Samal[8]. Commonest age group affected was 5-7 years and we could not demonstrate lymphadenopathy in our patients as was seen in the study done by Rath et al[9]. Both sexes were equally affected in contrast to the study reported by Rath et al[9]. In clinical practice the physical conditions that cause an individual to sickle are often unknown, but infection, dehydration, hypoxia and cold may play a part[10], some of these factors were applicable to those of our patients who got admitted during winter season and the patient who migrated from low land area (Gizan) to high land area (Khamis Mushayt). El Mouzan et al. in two group of patients observed that S.C.D. patients of Southwestern region had more severe clinical features consistently low Hb. levels and higher reticulocyte count suggesting more severe haemolysis as compared to the patients originating from Eastern region of Saudi Arabia. Thus causing more morbidity in the first group as compared to the mild form of second group, this has been attributed to high % of Hb. F interaction between Hb. S, Thalassemia and G6Pd deficiency, similar pattern of clinical features were also seen in our study confirming their observations[11]. Transfusion of normal red blood cells can provide symptomatic relief and prevent further complication[12], we had 34 (54.83%) symptomatic patients with Hb. less than 7 gram. in whom blood transfusion resulted in rapid improvement. Twenty three (37.09%) of our patients were underweight. By mid childhood most of the sicklers are underweight[13]. Gall stones with S.C.D. is a feature of adults and rare in children[14], we had one male child in whom gall stone was detected by ultrasonography.

Children with S.C.D. are prone to osteomyelitis which may be usual bone infecting organisms like salmonella or haemophilus influenzia[13], in contrast to Opawoye et al study[15] only two of our patients had bone involvement. Blood culture for both of these patients yielded no growth. The leucocyte count in our patients was higher, partly due to the infection, West et al reported that the leucocyte count in S.C.D. is higher than in normals[16]. This can be explained as majority of our patients belonged to high altitude or migrated from low altitude to high altitude which is known to have high blood indices. Radiological changes in bones like osteomylitis has been reported in S.C.D.[17]. No radiological changes were seen in our two patients who had bone involvement due to infection. One of our patient developed cerebrovascular accident and the lesion was detected by M.R.I. Stroke is a catastrophic complication of Sickle Cell Anemia that affects 6 to 17% of children and young adults, either as a result from occlusion of major cerebral vessels and affects children from 2 to 15 years of intracerebral or subarachnoid haemorrhage and affects older children[12], site of the lesion is detected either by CT scan or M R I[18]. Average stay in the hospital was five days. Higher mortality (12.5%) has been reported[19,15] in children with S.C.D. while in our study there was no mortality reflecting the improvement in the living condition, early diagnosis and prompt management of these patients due to existing S.C.D. programme in this region. Improved prognosis in this disease has also been noticed in U.S.A. due to better living conditions, adequate nutrition and medical care[3]. Less than 40% of our patients came for follow up. Follow up patients had less complications. There is a need to reinforce the efforts of S.C.D. programme already in existence to detect the new cases of S.C.D. and educate the families. Use of pencillin prophylaxis during first 5 years of life coupled with both pneumococcal and H. influenza vaccine in these patients should be implemented to prevent infective complications of this disease[20]. To encourage the research work and trial of newer drugs in this disease[21], such type of high altitude study should be undertaken and compared with that of the low altitude.

Table-II:

	Hemoglobin %	Number of patients	Percentage
1	Less than 7 gm.	35	56.45
2	Less than 10 gm	25	40.32
	Total	60	96.77
	Total leucocyte count 10/L	Number of patients	Prcentage
1	More than 20,000	23	37.09
2	10,000 - 19,999	29	46.77
	Total	52	83.87

Acknowledgments

We would like to thank the staff of the department of pediatrics Khamis Civil Hospital for their help & cooperation and Prof. Omer Saleh Zogabi. Ex. Director General Ministry of Health Aseer region of Saudi Arabia, for giving us permission to undertake this study.

References:

1. Weatherall D.D.J.; Some aspects of the haemoglobinopathies of particular relevance to Saudi Arabia and other parts of the Middle East. Saudi Med j, 1988;9(2):107-15.
2. El Hazmi M.A.F.; Haemoglobinopathies, Thalassemias an Enzymopathies in Saudi Arabia. Saudi Med. J. 1992;13(6):488-99.
3. Warsy A.S. El Hazmi M.A.F. Bahkim H.M.: Molecular therapy of Sickle cell Anaemia, the state of the art. Saudi Med J, 1985; 6(3):257-63.
4. Fuller J.: Sickle cell Disease and Thalassaemia, The Practitioner East Mediterranean Edition, 1995;6(1):51-4.
5. Serjeant G.R.; Thje challenge of Sickle cell disease in Saudi Arabia. Ann Saudi Med. 1990, 10(4):443-48.
6. Opawoye A.D.; Sickle cell anemia in Fifa. The practitioner Eas Mediterranean Edition, 1994;5(6):460-62.
7. El Hazmi M.A.F.; Haemoglobinopathies in Saudi Arabia, Saudi Med J. 1989;10(2):161-63.
8. Samal G.C. Sickle cell crisis Haemotological changes. Indian Pedfiatr. 1985;2(22):121-24.
9. Rath B K. Parija A C. Sen S K. Clinical profile of sickling disorders with reference to Genotype Phenotype Association. Indian Pediatr. 1982;4(19):327-31.
10. Darbyshire P.; Sickle cell disease in The U.K.; The Practitioner East mediterranean Edition, 1991;2:445-7.
11. El Mouzan M I. El Away B H. Al Turki M.T. Niazi G A.; Variety of Sickle cell disease in the Eastern Province of Saudi Arabia. J Pediatr 1989;114:973-6.
12. Lukens J N; Sickle cell Anemia. Winterobes clinical Haemotology, Lea & Febige, Philadelphia London, 9th ed. 1993;1068-84.
13. Hoing G R; Hemoglobin Disorders. Nelson Text Book of Pediatrics (Indian Edition), Prism Books Pvt.Ltd. Banglore India. 1996;15:1396-1400.
14. Al Salem A. H. Jaber A. Abu Srair H. Al Jama A. Al Jishi N.; Cholelithiasis in Saudi patients with Sickle Anemia. Ann Saudi Med, 1992;12(4):387-90.
15. Opawoye A.D. Haque T. Singh Y.; Bacteroal infections in Sickle cell patients. The Practitioner East Mediterranean Edition, 1996;7(4):225-27.
16. West M.S. Wethers D. Smith J. Steinberg M.; Laboratory profile of Sickle cell Disease, a cross sectional analysis. J Clin Epidemol, 1992;45(8):893-909.
17. Al Dabbagh A A. Acquaye J.K. Al Baghdadi T m. El Zamzamy M M.; Raiological bone changes of Sickle cell anemia in Western Saudi Arabia. Saudi Med J. 1989;10(5):367-71.
18. Annobil S H; Omojola M F; Adzaku F K; Addae S K; Mohammaed S; Cerebrovascular accidents (Strokes) in children with Sickle Cell Disease residing at high and low altitudes of Saudi Arabia. Ann-Trop-Paediatr. 1990;10(2):191-8.
19. Blakaran B; Char G; morris J S; Thomas P W; Serjeant B E; Serjeant C R; Stroke in a cohort of patients with homozygous Sickle Cell Disease. J Peditr. 1992;120(3):360-6.
20. Hatton C S R. Weatherall D.; Congenital Haemolytic Anemias. MEdicine International, Middle Eastern Edition, 1991;96:4005-9.
21. Rodgers G P.; Recent approaches to the treatment of Sickle cell anaemia JAMA, Middle East. 1992;2(1):53-7.

POLCYTHEMIA IN KASHMIRI NEWBORNS

Rashid Hameed M.D.; Mushtaq Ahmad M.D.; Wajid Ali M.D.; Muzaffar Jan M.D.;
Bhat Mushtaq M.D.; Charoo Basheer M.D.; Masood-ul-Hassan M.D.

***Abstract:** Neonatal polycythemia defined as a venous hematocrit greater than 65% is the primary cause of hyperviscosity in newborn infants. Polycythemia and hyperviscosity may have lasting effects in brain, heart, kidney and intestine and approximately 40% of babies may have long term neurological sequalae.*

***Key words:** Polycythemia; Hyperviscosity, Hematocrit.*

JK-Practitioner 1999; 6(4):299-301

Subject & Methods

900 neonates born in Lal-Ded Hospital were screened. Detailed antenatal history, type of delivery, weight recording and gestational assesessment physical and neurological criteria were recorded.

Capillary heel stick hematocrit was determined on all neonates between 2 and 4 hours after bith. A venous hematocrit was performed, if the capillary hematocrit was 65% or more. The infants were considered to be polycythemic if venous hematocrit was 65% or more. A repeat hematocrit at the age of 24 hours (or at any age, if symptoms appeared) was done if initial hematorcit was higher.

Under all aseptic precautions heel was warmed and prick given by a disposable needle and blood letting done without squeezing the site. Venous samples were taken if capillary PCV was 65% or above (capillary PCV is 6-7% higher than venous PCV). Under aseptic precautions twenty four number disposable needle was inserted into antecubital vein and blood letting done into the microtube. Blood was allowed to enter the microtube by capillary action and PCV percentage was done. Microtubes used were 75mm length and 1mm of internal diameter. 15mm were left unfilled and tube blocked on one side by wax. Tube was put into the hematocrit centrifuge and centrifuged for 5 mts. Reading was directly obtained from scale lying by the side of capillary tube in the microcentrifuge. Reading corresponding with the upper level of the packed volume of cells was taken as PCV percent.

A detailed clinical examination was done within first twelve hours of age. The various signs and symptoms, which were found in polycythemic babies were plethora, lethargy, tachypnoea, tachycardia, jitteriness, convulsions and feeding problems.

Polycythemic babies were divided into two groups - first group of symptomatic babies and second group of asymptomatic babies. Therapeutic intervention in the form of partial exchange transfusion was done in symptomatic babies. No intervention was done in the asymptomatic babies. Partial exchange was done with plasma,the volume of which was calculated with the following formula[3].

$$\underset{\text{to be exchange}}{\text{volume (ml)}} = \frac{\text{Observed venous hematocrit - desired venous hematocrit}}{\text{Observed venous hematocrit}} \times \text{Blood Volume}$$

$$\text{Blood volume (ml)} = 85 \times \text{wt. in kgs.}$$

Method of partial exchange transfusion

It was performed in the nursery ward with due aseptic precautions. The baby was kept adequately warm during the procedure with the help of an overhead radiant heat source. The stomach contents were aspirated. Baby was fastened on a well-padded splint and stethoscope attached to baby's precordium to monitor cardiac status. An exchange transfusion test was prepared incorporating the following information: In/out volume, heart rate, respiratory rate, colour of baby, drugs administered and any other problem encountered.

After full aseptic precautions umblical vein was catheterized until free flow of blood was obtained. The catheter was attached to a three way connecting to syringe, plasma and the waste container. The blood was withdrawn with gentle suction in aliquotes of 10-20 ml and replaced by same amount of plasma till desired amount reached. Pre and post exchange blood samples were taken for packed cell volume estimation. Catheter was removed, umbilical stump sprayed with antibiotic

---

From the Department of Neonatology & Critical Care Pediatrics, SKIMS, Soura, Srinagar (India) (Hameed, Ahmad, Ali, Jan, Bhat, Charog, Prof. Hassan)

Received February 1999 Accepted July 1999

Correspondence to : Dr. Mushtaq Ahmad Shameem-Ashiana, SK Colony, Anantnag, Kashmir 192 101 (Islamabad)

powder and aseptic dressing applied. Prophylactic antibiotics were given.

Results

Out of 900 neonates 35 (3.8%) had polycythemia, out of which 10(28.57%) were preterm (<37 wks), 24(68.55%) were term (37-42wks) and 1(2.85%) post-term (more than 42 wks) (Table I). 20(57.25) were male and 15(42.8%) were female. Out of 35 babies 8(22.8%) were symptomatic and 27(77.2%) were asymptomatic.

Mean hematocrit of polycythemic neonates in case of symptomatic babies was 74.37±2.23 and in those asymptomatic babies 68.55±2.04 (p value of < 001). Mean hematocrit of the polycythemic neonates at 2-4 hours age was 69.77±3.07%% (p value <.001) and at 24 hours age was 58.23±2.06% (p value .05) (table II).

Table-I:

Number of neonates	No(%) with polycythemia
900	35(3.8%)
Gestational age:	
Preterm (<37 wks) 130(14.4%)	10(28.57%)
Term (37 - 42 wks) 760 (84.4%)	24(68.55%)
Post-term (>42 wks) 10(1.1%)	1(2.85%)

Discussion

Incidence of polycythemia varies from place to place because of varying altitude. Kashmir is geographically and climatically different from the rest of the country having an altitude of about 5200 ft. from the sea level.

Out of 900 neonates screened 35(3.8%) had polycythemia while incidence observed by Sing S et al (1920) was 3.06%[4]. The incidence observed from the other parts of world varies from 0.45% to 4.0%. In Denver, having an altitude of 1612 meters the incidence of polycythemia was found to be 4% by Wirth (1979). In Virginia, which is at sea level Stevens K (1980) observed the incidence of neonatal polychythemia as 1.8%[2].

Polycythmia is commonly associated with small for gestational age babies. In our study 21(60%) polycythemic babies were small for gestational age. Similar were results of Sing M et al(1990).[5] This high incidence of polycythemia is small for gestational age babies could be because of increased erythropoitin secondary to chronic hypoxia. In our study 10(28.15%) neonates were appropriate for age as is seen by other workers. 4(11.4%) babies in our study were large for gestational age which is in confirmity with other studies[6]. So our study is in confirmity with those of other studies with respect of growth status. In our study 24(68.5%) neonates were fully term, while a value of 77.8% and 70% was observed by others[5,6]. In our study 2.8% were post term, while other studies showed 28.5% neonates having polycythemia were preterm, while a percentage of 26 and 18 was observed by others[2,4,5]. So our study of polycythemia in neonates is in confirmity with those of others will respect of gestation age.

The mean hematocrit of polycythemic babies who were symptomatic was 74.37±2.33% (range 70-78%) and for asymptomatic babies 68.55±2.04 (rage 66-75%) at 2-4 hurs of age (p<.001). Other studies showed 65-80% hematocrit[8]. We found that a majority of polycythemic babies were asymptomatic (77%) and 23% were symptomatic. Others found a figure of 70.4% and 54%. In our study symptoms developed within first 24 hours of age as is seen by other workers[4,5].

Varrious signs and symptoms observed in our study were feeling problem in 20%, plethora in 20%, lethargy in 8%, jitteriness in 8%, convulsions in 8% and tachypnoea in 6% of cases. Similar were observations made in other studies[6].

Partial exchange transfusion improved the signs and symptoms within first 24 hours and they were indistinguishable from asymptomatic group within next three days. In another study symptoms were relived within 8-20 hrs[4]. We did partial exchange in symptomatic babies only and in those asymptomatic babies who developed symptoms which is in confirmity with other studies. No therapeutic intervention was made in asymptomatic babies. Polycythemia when symptomatic and treated in time will prevent lot of morbidity and mortality in the neonates and its long term sequalae can be prevented by simple intervention of partial exchange transfusion.

Table-II;

No. of polycythemic neonates		35(3.8%)
Sex	Male	20(57.2%)
	Female	15(15(42.8%)
Symptomatic		8(22.8%)
Asymptomatic		27(77.2%)
Mean hematocrit		
	Symptofmatic	74.37±2.23 p<.001
	Asymptomatic	68.55±2.04 p<.001
	Age : 2-4 hrs	69.77±3.07% p<.001
		24 hrs - 58.23±2.06 p<.05

References:

1. Hathaway WE. Neonatal hyperviscosity. Pediatr 1983,72:562-569.
2. Stevens K, Wirth FH. Incidence of neonatal hyperviscosity at sea level. J Pediatr. 1980;97:118-119.

3. Singh M. Polycythemia and hypervicosity. Care of Newborn 3rd edition 1985;335-336.
4. Singh S, Singh P, Paul UK et al. Polcythemia in newborn. Do asymtptomatic babies need exchange transfusion. Indian Pediatrics 1990;27:61-65.
5. Singh M, Singh P, Paul UK et al. Polycythemia in newborn. do asymptomatic babies need exhange transfusion. Indian Pediatrics 1990;27:61-65.
6. Wishwell TE, Cornish JD, Northam RS. Neonatal polycythemia-frequency of clinical manifestations and other association findings. Pediatrics 1986;78:26-30.
7. Goldberg K, Wirth FH, Hathaway WE et al. Neonatal hyperviscosity II, effects of plasma exchange transfusion. Pediatrics 1982;69:419-425.
8. Ramamurthy RS, Brans YW. Neonatal polycythemia criteria for diagnosis and treatment. Pediatrics 1981;68:168-174.

With Best
Compliments from

KASHMIR PHYSIOTHERAPHY
&
REHABILITATION CENTRE

HRDC CAMPUS, POST OFFICE LANE, RAJBAGH, SRINAGAR-8
TELE : 450920

HELLP SYNDROME:
A CASE STUDY WITH REVIEW AND RECOMMENDATIONS

Abid Bhat, M.D.; Khalid J. Qazi, M.D., F.A.C.P.

Abstract: *In 1982, Weinstein described the syndrome of hemolysis, elevated liver enzymes and low platelet count (HELLP) and considered it a unique variant of preeclampsia.*[1] *Clinicians continue to be confused by this condition because of the lack of standardized diagnostic criteria, and its varied presentation. The onset of symptoms may be prenatal, but cases have occured up to seven days post natally without any antecedent preeclampsia.*

Key words: *HELLP Syndrome; Pre-eclampsia*

JK Practitioner (1999;6(4):302-304

Case Study:

A 16 years old Hispanic primigravida with an estimated gestational age of 32 weeks presented to the emergency department with the chief complaints of right upper quadrant (RUQ) pain for 2 days. Pain was described as burning in character with no radiation or relation to the food intake. The patient denied nausea, vomiting, diarrhea, itching, fever, cough, chest pain, shortness of breath, oliguria, dysuria or swelling of feet. The prenatal history was uneventful except for urinary tract infection at 20th week of gestation, which was treated successfully with antibiotics. She denied history of smoking, alcohol intake or iv drug abuse.

On examination, the patient's height was sixty six inches and weighed 205 lbs. She was afebrile. Blood pressure was 150/85mmHg and heart rate 82/min. There was no icterus, lymphadenopathy or thyromegaly. Cardio-respiratory examination was normal. Abdomen was soft with mild tenderness in RUQ but no rebound tenderness. The liver or spleen was not palpable. Fundal height corresponded to 32 weeks gestation. Fetal heart tones were audible at 140-153/min with a Doppler stethoscope. The rectal exam was heme negative. Slight pedal edema was noted.

Neurological examination including deep tendon reflexes were normal. Initial lab tests including creatinine, electrolytes and glucose were normal. Admission liver enzymes were also normal with AST of 38 U/lt, ALT 40 U/lt, alkaline phosphates 173 U/lt and total bilirubin 0.2mg/dl. Amylase and lipase were normal. WBC count was 10,300/ul, Hb 12gm/dl, HCT 35.9% and platelet count 170,000/ul. Prothrombin time was 12.2 sec with INR of 0.9. Urinanalysis was also normal. Abdominal and pelvic sonogram revealed single and viable pregnancy.

The patient was admitted to the hospital and treated symptomatically with complete bed rest. However, the patient continued with upper abdominal pain. Repeat BP was 170/100mm Hg. Lab studies within 12 hours revealed AST of 659 U/l and ALT 469U/l. Platelets had dropped to 97,000/ul. Urinanalysis now revealed 3+proteinuria. The diagnosis of HELLP syndrome was made. Patient started on hydralazine for hypertension and magnesium for seizure prophylaxis. Induction trial was attempted but failed. Third set of lab studies done after four hours of the second set revealed AST of 2276u/l and ALT of 1992u/l. Platelet count was now only 49,000/ul. Emergency cesaerian section was done. A live baby was delivered with an Apgar score of 6 and 7 at 1 and 5 minutes respectively. By the third post operative day, patients' BP was 130/80 mmHg, AST 129 u/l, ALT 203u/l, platelet count 113,000/dl and Hb of 10.2mg/dl. The patient continued to improve and was discharged home 5 days after delivery with both the baby and the mother in good condition.

Discussion

Hemolysis for the diagnosis of HELLP syndrome was defined by Weinstein by the following: schistocytes or Burr cells on peripheral smear with a total bilirubin greater than 1.2 mg/dl, or lactate dehydrogenase greater than 600 IU/lt.[2] Liver enzymes are considered elevated when the AST is greater than 50 IU/lt[3] and thrombocytopenia is defined here as platelets of less than 100,000/dl[4]. The incidence of HELLP syndrome in preeclampsia ranges from 2% to 12%[5]. The incidence

---

From the Sisters of Charity Hospital, Buffalo, New York (Qazi, Bhat) **Internal Medicine Section.**

Received August 1999 Accepted September 1999

Correspondence to : Dr. Khalid J. Qazi, M.D., Chairman & Program Director Internal Medicine Sisters of Charity Hospital Buffalo, NY.

appears to be higher in cases of preeclampsia that have been managed conservatively.

The pathogenesis of this serious condition still remains an engima. The common link appears to be endothelial cell injury with subsequent vasospasm, platelet activation, an abnormal platelet prostacyclin-thomboxane ratio and decreased release of endothelium-derived relaxing factor. Activated protein C resistance resulting from a mutation in coagulation factor V has now emerged as the leading cause of thrombosis in pregnancy and recent data links the HELLP syndrome with factor V R5060 Q mutation[6]. Since HELLP syndrome is a severe form of preeclampsia, the risk factors are essentially the same, i.e., primigravida, young maternal age, advanced gestational age, chronic hypertension, diabetes, multiple gestations and previous preeclampsia. In more recent years, microangiopathic, hemolytic anemia is considered the hallmark in this condition[7]. Bone marrow studies show increased number of megakaryocytes, a feature that is compatible with either increased platelet consumption or excessive destruction[8].

The classic presentation involves epigastric or right upper abdominal pain with nausea and vomiting. Less common clinical presentations include convulsions, jaundice, gastrointestinal bleeding, hematuria or bleeding gums[9]. Hypertenstion and proteinuria may be absent further complicating the picture[10]. The perinatal mortality is reported to range from 7.7% to 60% and maternal mortality from 1 to 24%[11]. Serious complications include disseminated intravascular coagulation, abruptio placenta, acute renal failure, ascites, hepatic capsular rupture, pulmonary edema, pleural effusion and fetal or maternal death. The clinical presentation can be easily confused with many different clinical entities (table 1).

Table 1: Medical and Surgical disorders confused with HELLP Syndrome

- Acute fatty liverr of pregnancy
- Appendicitis
- Diabetes insipidus
- Gall bladder disease
- Hepatic encephalopathy
- Hemolytic uremic syndrome
- Glomerulonephritis
- Hyperemesis gravidarum
- Idiopathic thrombocytopenia
- Kidney stones
- Peptic ulcer disease
- Viral hepatitis
- Thrombotic thrombocytopenic purpura
- System lupus erythematosus

Managementof HELLP syndrome includes control of hypertension, seizure prophylaxis, coagulation monitoring and delivery, preferably in a tertiary care centre. Labetalol or hydralazine can effectively lower blood pressure. Nifedipine has been used by some with equal efficacy but is not the preferred agent. A satisfactory responses is defined as DBP between 95 and 100 mm hg; DBP should not be lowered any further since placental perfusion may be compromised. Seizure prophylaxis is achieved with intravenous magnesium. The therapeutic goal of magnesium is to achieve a serum level of 4-6 mg/lt. Because IV magnesium infusion carries the risk of CNS and respiratory depression, Calcium gluconate should be available at the bedside. Blood products may be needed to reverse the thrombocytopenia, and anemia.

The obstetrical management consists of initial stabilization and delivery. If the gestational age is less than 24 weeks, fetal outcome is universally poor and immediate delivery is advocated. If the fetus is greater than 34 weeks old, the outcome is usually favourable with prompt delivery. In the rare circumstance when the fetus is between 24 and 34 weeks old, conservative management may be considered for a short period of time. However, if there is evidence of maternal or fetal distress, however mild, immediate delivery is manadatory.

Controversy still exists regarding the optimal method of delivery for patients with HELLP syndrome. Historically, Caesarean section has been advocated as the primary method especially when evidence of labor or cervical ripening is lacking[12]. More recently, this approach has been challenged with series of successful vaginal deliveries in such patients so that a C-section is no longer considered mandatory[2].

Conclusion:

The complaint of RUQ pain in a pregnant patient requires careful consideration of life threatening complications espeically eclampsia and the HELLP syndrome. Hypertension and proteinuria in a gravid female represent preeclampsia unless proven otherwise. The diagnosis of HELLP syndrome should be entertained in any pregnant female with evidence of elevated liver enzymes with hematological manifestations of thrombocytopenia and/or hemolysis. Early recognition and aggressive management is essential for a healthy outcome of the pregnancy.

References:

1. Weinstein L. Syndrome of hemolysis, elevated liver enzymes and low platelet count: A severe consequence of hypertension in pregnancy. An I Obstet Gynecol. 1982;142:159-167.
2. Sibai BM, Anderson GD. Hypertension. In: Gabbe SG, Niebyl JR, Simpson JL, eds. obstetrics: Normal and problem pregnancies, 2nd Ed. New York: Churchill Livingstone, 1991;993-1055.
3. Sibai BM, Ramadan M, Usta I, Salama M, Mercer B, Friedman S. Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP

syndrome). Am J. Obstet Gynecol. 1993;155:501-9.

4. Fagan GA. Diseases of liver, biliary system and pancreas. In: Creasy R, Resnik R, and Eds. Maternal fetal medicine: principles and practice, 3rd ed. Philadelphia: W.B. Saunders Co; 1994; 11041-61.
5. Sibai BM, Taslimi MM, El-Nazer A, Amon E, Mabie BC, Ryan GM. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes and low platelets in severe preeclampsia-eclampsia. Am J Obstet Gynecol. 1986;155:501-507.
6. Brenner B, Lanir N, Thaler I. HELLP syndrome associated with factor V R 506 Q mutation. Br J Haematol 1996;92:999-1001.
7. Brain, MC, pacie JV, Hourihane DOB: Microangiopathic hemolytic anamia: The possible role of vascular lesions in pathogenesis. Br J Haemo Morning Reporttol 1962;8:358.
8. Thiagarajah S, Bourgeois FJ, Harbet GM, et al: Thromboocytopenia in preeclampsia: Associated abnormalities and management principles. Am J. obstet Gynec 12984 150:1-7.
9. Sibai Bm. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much to do about nothing? Am Journal of Obstet Gynecol. 1990;162:311-316.
10. Schwartz ML. Brenner WE. Pregnancy induced hypertension presenting with life threatening thrombocytopenia. Am J Obstet Gynecol. 1983;146:756-759.
11. Kenneth A. Jones: Severe HELLP Syndrome presenting with Acute gum bleeding following tooth brushing at 38 weeks gestation. American J of critical care 1993; 2 : 5.
12. Fairlie FM, Sibai BM. Hypertensive diseases in pregnancy. Reece EA, Hobbins JC, Mdahoney MJ, Petrie RH, eds. Midicine of fetus and mother. Philadelphia: J.B. Lippincott Co; 1992;925-42.

Giant Recurrent Ventral Hernia (A Surgical Challenge)

Shabir Iqbal, MS; M.Ch.; A. Qayoom Lone, M.D.; I. Naqash, MD.; Riaz A. Wani, MD; S. Zahid, M.B.B.S.; K. Alam, M.S.

Abstract: *For Giant Ventral Hernias in which primary repair is impossible or has failed and where definitive correction by prosthetic (Marlex) mesh has given way, can be helped by using patients own vascularized tissues for reconstruction such as TFL (Tensor Fasciae Latae) myofascial unit as described in this article.*

Key Words: *Tensor Fasciae Latae, Poly - tetraflouroethylene*

JK-Practitioner 1999; 6(2):305-307

Introduction

The pathophysiology of giant ventral hernias includes reduction in the capacity of abdominal cavity by scar contracture of flank muscles, massive musculofascial defects in abdominal wall sometimes extending from xiphisternum to the pubis, obesity and infiltration of fat into fascial planes further militates against a successful repair by any of the ordinary methods. Patients and surgeons alike are discouraged by repeated and often unsuccessful attempts at repair. Use of synthetic materials such as Marlex mesh, Dacron mesh and others have proved largely inadequate due to being inelastic and their significiant infection and rejection rate. This case report illustrates that even after wide scaring following previous surgical attempts and use of prosthetic mesh and despite huge obesity reconstruction can be achieved using tensor fasciae latae (TFL)myofascial flap.

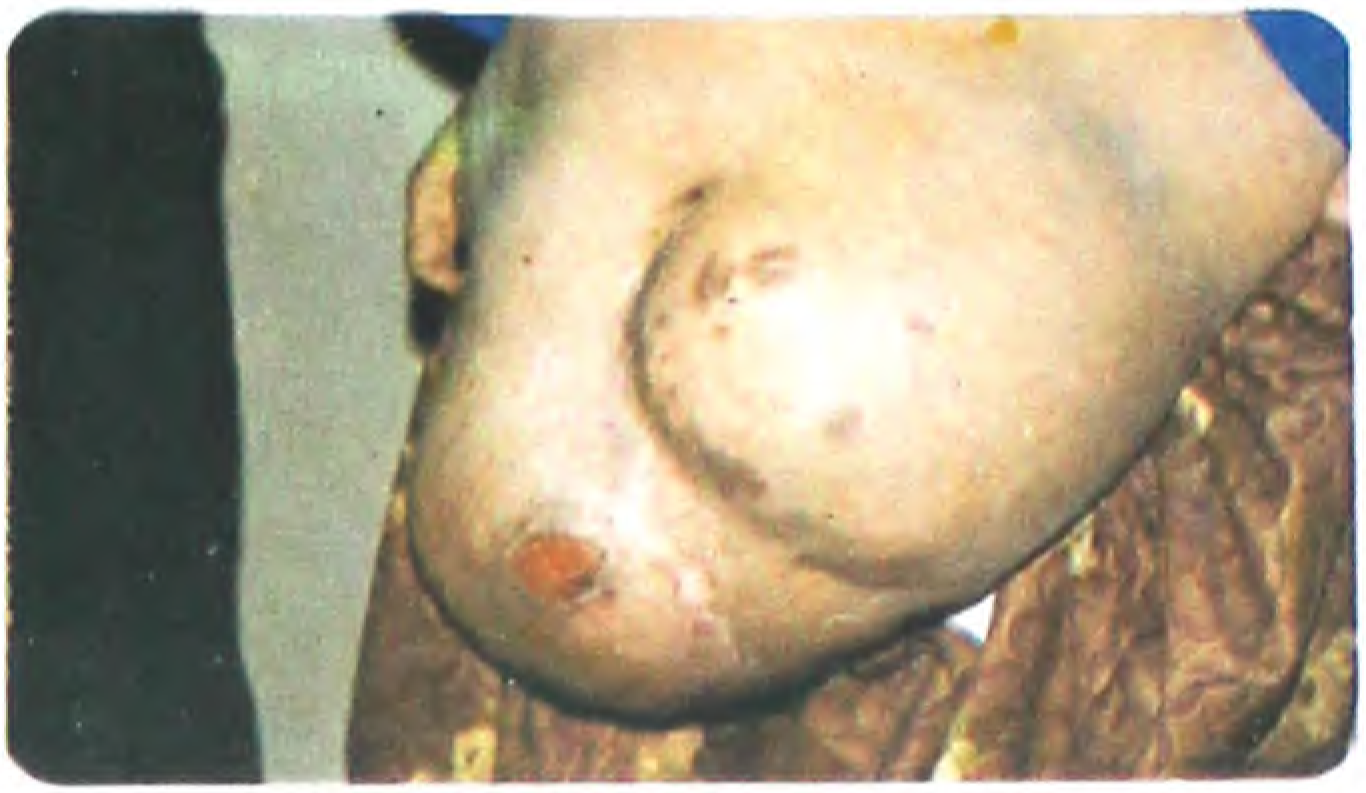


Fig.I: Pre Operative view of a huge ventral. Hernia and recurrent Skin Ulcers.

Case Report

A 65 year old lady presented with a huge ventral hernia for last 7 years. There was extensive scaring of whole lower abdomen with multiple incision marks and skin ulcers (Figure I). The size of hernial sac was so huge that in standing position it was reaching almost to the knees (Figure III) and creating a picture of two abdominal cavities.

History revealed that patient had undergone hysterectomy through midline lower abdominal incision about 8 years earlier by a Gynaecologist. She developed an incisional hernia which she noticed about one year after surgery. Its size went on increasing. She was advised to use external abdominal supports by general surgeon. A year later the general surgeon treating the patient attempted an anatomical repair of the defect. The operation was not successful and again patient developed a hernia within 3-4 months after surgery. At this stage patient was referred to our institute, where she was being followed up by another general surgeon. She was using external abdominal supports. Another attempt of surgical repair was made, using Marlex mesh to supplement the deficient fascial structures, by a senior surgeon about 3 years after previous surgery. Patient remained well for 5-6 months but some serous collection continued for three months and about few months later same huge sac appeared. At this stage patient got very much depressed and her morale was very low. She thought her problem looks to be incurable. However, after about 3 years from 2nd surgical attempt it was unbearable for her as she was almost bed restricted. She could not perform any of her daily activities and life was made miserable by further

From the Departments of Plastic & Reconstructive Surgery (Iqbal); Anaesthesiology (Lone, Naqash, Wani) and Department of General Surgery (Wani, Zahid, Alam) **SKIMS, Soura, Srinagar, Kashmir, India**

Received June 1997 Accepted March 1999

Correspondence to : Dr. Shabir Iqbal, Assistant Professor, Department of Plastic & Reconstructive Surgery, SKIMS, Soura, Srinagar-11, Kashmir, India. Post Bag No. 27

increase in size of sac and non-healing ulcers on the sac giving pus and bloody discharge all the time. At this stage plastic surgeons were called for help and challenge was taken considering the miserable condition of the patient.

Operative Procedure:

After making an elliptical transverse incision that encompassed the entire hernial sac, including all scars and skin ulcers, we carefully freed the subcutaneous tissue from the hernial sac. The apponeurotic fascia all around the hernial sac was exposed for a distance of at least 5-6 cms. At this stage hernial sac was opened and abdominal contents reduced, redundant omentum excised and adhesion lysed and sufficient margins of peritoneum preserved and separated from healthy posterior wall of fascia for suture placement later on. The hernial sac was excised along with unhealthy skin and previous Marlex mesh which had folded towards one end. The peritoneum was closed over the peritoneal contents. At this stage assessment of fascial defect was made both in length and width and tensor fasciae latae myofascial unit planned for healthy reconstruction of the huge apponeurotic fascial defect (Fig. II) which could not have been closed primarily and where use of Marlex mesh had already failed. The planning was done in reverse several times before elevating the flap. The anatomy of this flap as well as its elevation has been sufficiently described by Nahai F (1979) as also by Wangensten (1934 & 1946). The tensor fasciae latae (TFL) Myofacial unit was bared on its single pedicle the transverse branch of lateral femoral circumflex artery which is 6-8 cms. below anterior superior iliac spine. If one draws a line passing from greater trochanter to the mid-lateral aspect of knee, this line should bisect the centre of tensor fasciae latae flap. An incision of sufficient length was made on the thigh on this line and flap of sufficient length and widh elevated and tunneled into the defect on abdominal wall (Fig. II) to have a tension free closure all around. However, minimal access endoscopic elevation of the flap can be achieved to avoid a big incision of thigh-K. Onishi (1997)[3].

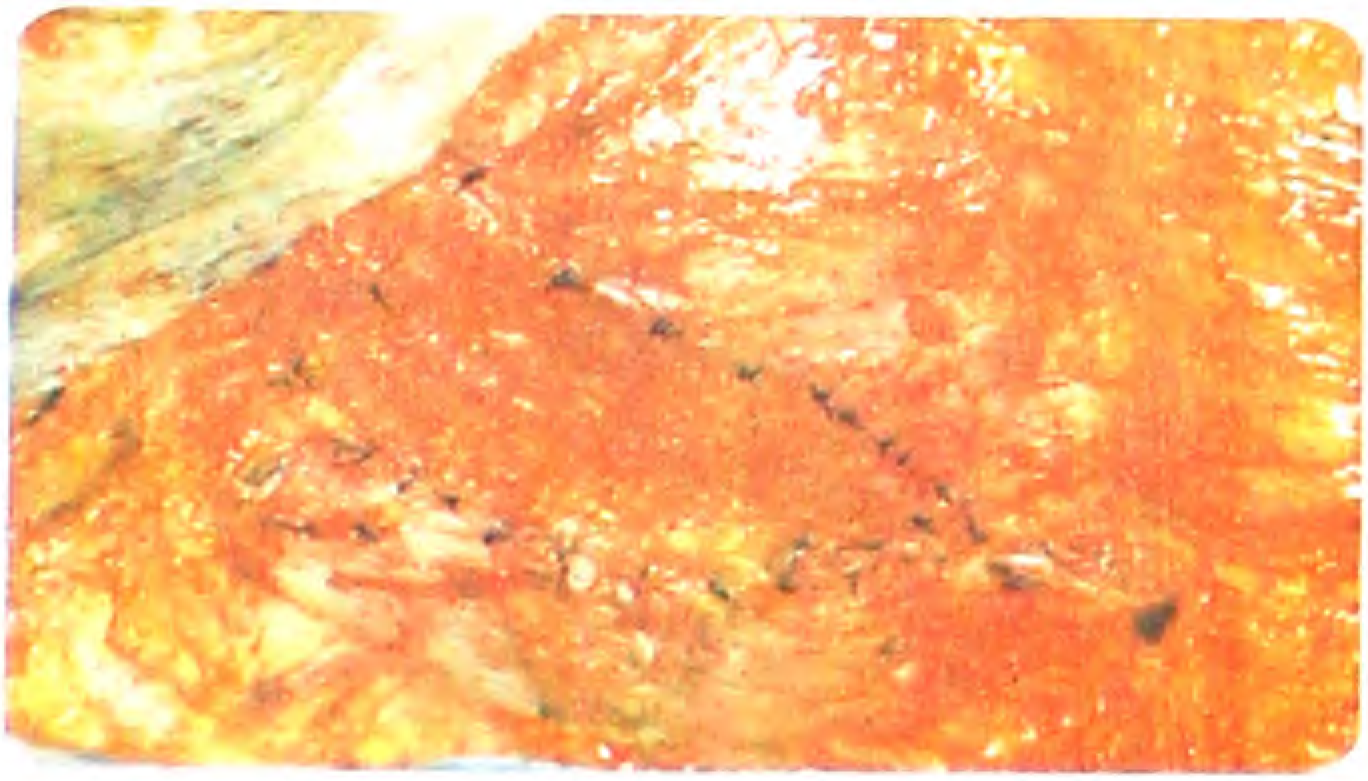


Fig.II: Inserting of TFL flap tunneled into abdomen from thigh.

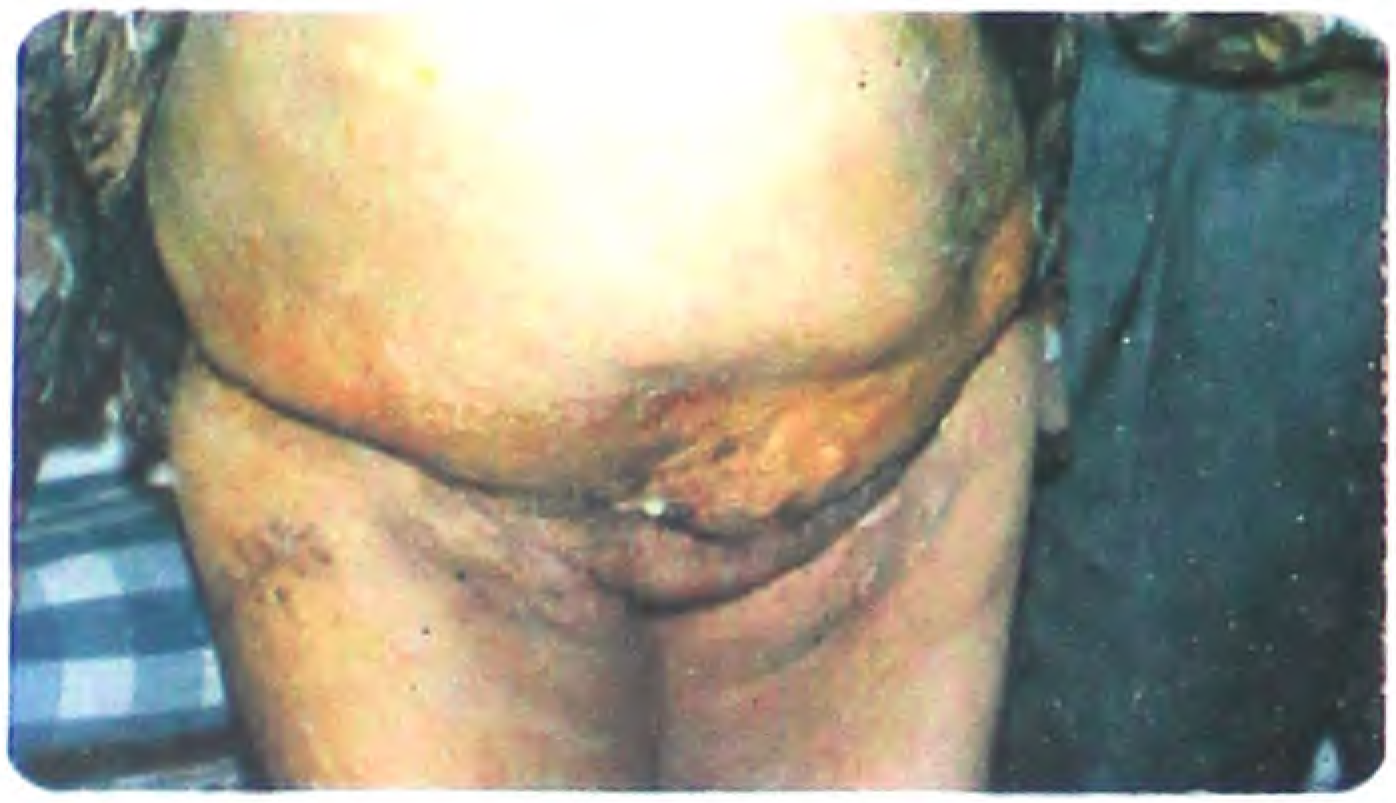


Fig.III: Excellent Postoperative results

The dead space under the skin flaps was drained by corrugated rubber drains and skin closed as in an abdominoplasty, suprapubic transverse incision. Thigh incision was also closed. Patient was asked to use an abdominal binder for 3-4 weeks post-operative. An excellent early post-operative result is well demonstrated in (Fig. III). The patient is on follow-up for last one year and there is no evidence of any recurrence.

Discussion

Complex, giant and recurrent ventral hernias are notoriously difficult to repair and are associated with high recurrence rate, about 44% in case of recurrent giant ventral hernias (Matapurkar 1991)[4].

Repair of such difficult hernias has been possible using various types of prosthetic material ranging from polypropylene mesh. Thamrongroj Temudon et al (1996)[5], Marlex mesh-R. G. Molloy (1991)[2] to expanded PTFE-Pedro A Rubio et al (1994)[6]. However surgeons have often been discouraged by high rate of infection and rejection of such materials as is also demonstrated in our case for skin is thinned out in the area and tissue defecits are huge. Repair by autogenous fascia has been most reliable and has been used for almost a century from Bassini's operation (1889) to McArthur (1901), Krischner (1909). Gallie and Le-Mesurier (1921) demonstrated use of fasciae latae autogenous grafts and Wantgensten (1934 & 1946)[2] later demonstrated the suitability of pedicled fascia latae flap. With advancements in technique of harvesting vascularised autogenous tissue flaps the complexity and size of tissue defects to be repaired also increased. Peter M.O Hare & Alan G Leonard (1982)[6] observed that tensor fasciae latae myofascial unit would survive upto almost the knee joint levels, so could be used for giant defects well beyond the limits of lower abdomen. The same fact has been confirmed by successful repair of huge defect in our case. it is also note worthy that such vascularised autogenous tissues can resist and face wound infections that may be unavoidable in such circumstances better than artificial prosthetic and costly materials.

References:

1. Nahai F, Hill HL and Hester TR. Experience with tensor fasciae latae flap. Plastic and Reconstrutive Surgery 1979; 63:788.
2. Wangesten OH. Repair of large abdominal defects by pedicled fascial flaps. Surgery Gynaecology and Obstretics 1946; 82:144.
3. Onishi, Maruyama Y, Yataka M. Endoscopic harvest of the tensor fasciae latae muscle flap. British Journal of Plastic Surgery 1997; 50:58-60.
4. Mata-Purkar BG, Gupta AR et al. A new technique of Marlex peritoneal sandwich in repair of large incisional hernias. World J Surg 1991; 15;768-70.
5. Thamrongroj Temudon, Mohammad Siadati and Michael G Sarr. Repair of complex or recurrent ventral hernias by using tension free intraperitoneal prosthetic mesh (stoppa technique). Surgery 1996; 120(4):738-744.
6. Pedor A, Rubio Giant ventral hernias : A technical challenge. Int Surgery 1994; 79:166-168.
7. Peter MO' Hare and Alan G Leonard. Reconstruction of major abdominal wall defects using the tensor fasciae latae myocutaneous flap. British Journal of Plastic Surgery 1982; 35:361-366.
8. Molloy RG, Moran KT, RP Waldron et al. Massive incisional hernia : abdominal wall replacement with Marlex mesh. British Journal of Surgery 1991; 78: 242-244.

ALBENDAZOLE THERAPY IN TYPE III HYDATID CYST LIVER

Yattoo G.N. M.D., D.N.B.; Thakar G.M. M.D.; Alai M.S.M.D.; Bhat F.A. M.D.;
Saleem S.M. Ph.D; Zargar S.A. M.D., D.M.

Abstract: *Medical Therapy is a safe and very cost Effective treatment of selective group of patients with Hepatic Hydatid Cysts. Five patients with type III Hydatid Cysts of the liver are reported after successfully treating them with albendazole.*

Key Words: *Hydatid Cyst; Liver; Albendazole therapy.*

JK-Practitioner 1999; 6(4):308-309

Introduction

Recently percutaneous drainage has been successfully used as an effective treatment modality for uncomplicated hepatic hydatid cysts[1]. When compared to surgery percutaneous drainage is not only equally effective treatment option but it also reduces the hospital stay and is cost effective[2]. However a major problem arises in the management of type III hydatid cysts wherein at times it becomes difficult to puncture and aspirate individual daughter cysts. Over a period of to years we treated five patients of type III hydatid cysts of Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir by using albendazole.

Material and Methods

Over a period of two years we collected five patients, three males, two females (age 37-52 yrs. mean 45 years) who had type three hydatid cysts of liver and were difficult to aspirate (n=3) or previous aspiration was incomplete (n=2). The diagnosis of hydatid cysts was made by typical ultrasonographic appearance (fig 1), positive Casoni's test and hydatid serology. After obtaining a formal consent from the patients, they were put on albendazole 15mg/kg/day in two divided doses for a period of six to ten months (mean 7 months) with one week was out period in each month. Patients were critically monitored for any bone marrow, hepatic or renal toxicity. All the patients had monthly follow up by ultrasound scanning and three monthly hydatid serology estimation.

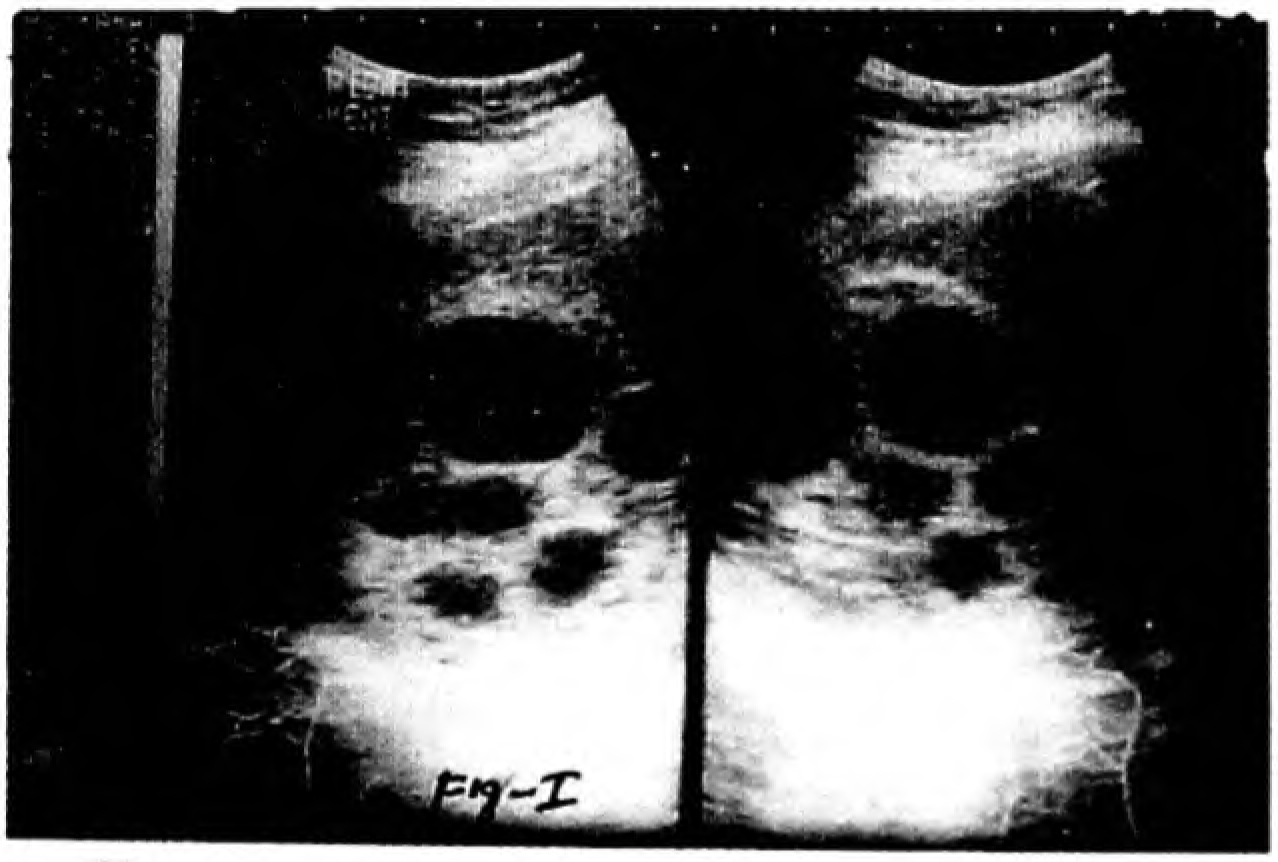


Fig. 1. Ultrasound scan of type three hydatid cyst (7x7cms) in the requt lobe of liver (before treatment)

Results

Four out of five patients with type three hydatid cysts showed progressive cyst regression and subsequent pseudotumour appearance at six to ten months (mean 8 months) follow up period after starting the treatment (Figures 2-4). One patient took longer time (12 months) for pseudotumour appearance. Hydatid serology showed a declining trend in all the patients six months after the treatment was started. None of the patients developed any drug related complication as evident by normal hepatic, renal and hematological parameters. Two patients developed mild right upper quadrant pain in the initial few weeks of treatment with spontaneous disappearance during the follow up.

Discussion

Our decision to treat patients having type three hydatid cysts with albendazole was based on the successful experience reported earlier[3]. Percuteneous drainage was not done due to technical reasons. Surgery was avoided because most of our patients in our centre are being treated by percutenous drainage. Surgery is reserved mainly for complicated cysts e.g., ruptured cysts

---

From the Department of Department of Gastroenterology, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar - 190011, Kashmir (India). (Thakar, Yattoo, Aali, Bhat, Saleem & Zargar)

Received July 1999 Accepted August 1999

Correspondence: Dr. G.N. Yattoo, Assistant Professor, Department Gastroenterology, Sher-i-Kashmir Institute of Medical Sciences, Soura, P.B. No. 27 Srinaga - 190011, Kashmir (India

in the biliary tree or infected hydatid cysts[4,5].

Albendazole produced sonographic evidence of cyst regression and pseudo tumour appearance in all our patients though one patient took longer to do so. Subsequent sonographic observation at three monthly follow up period showed no evidence of cyst recurrence, although it was too early to assess the long term results. The serological improvement in treated cases was also encouraging. Although albendazole therapy has not been recommended for prologned period of time[3], yet we took the risk of giving the treatment for 8-10 months without noticing any untoward hepatic, renal or haematological side effects.

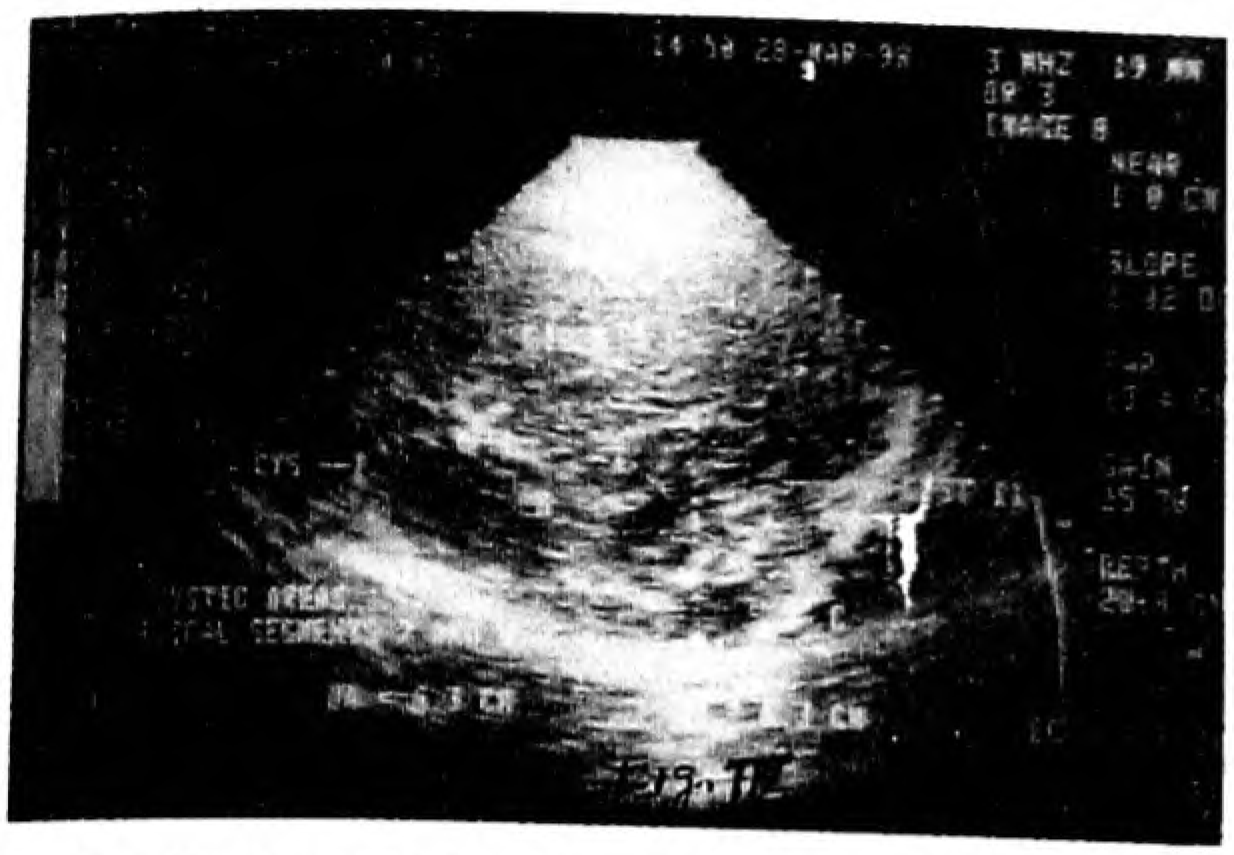


Fig. II. Ultrasound showing pseudo tumor appreance of the treated hydatid cyst (one year after trestment)

We concluded that albendazole therapy is an effective alternative for treatment of hepatic hydatid cysts which are not amenable to treatment by percutenous drainage, the treatment modality of choice at our centre and elsewhere not only for liver cysts but for hydatid cysts of other organs as well.

References

1. Khuroo MS, D.M; Nazir A. wani, M.S; Gul Javid, M.D.; B.A. Khan, M.D; Ghulam N. Yattoo, M.D; Altaf H. Shah, M.D. and Samoon G. Jeelani, M.D. Percutaneous drainage compared with surgery for hepatic hydatid cysts.NEJM. 1997, 337, 13, 881-886.
2. Khuroo MS, Zargar SA, Mahajan R. Echinococcus granulosis cysts in the liver, Management with percutaneous drainage. Radiology 1991;180, 141-5.
3. Moris DL, P.W. Dykes, B Dickson SE Marriner et al. Albendazole in hydatid disease. BMJ, 286, 103-104, 1983.
4. Hanson JR; Management of complicated hydatid cysts. Ann Surg. 158: 1020-1034, 1963.
5. Khuroo MS, Dar MY, Yattoo GN, et al. Percutaneous drainage versus albendazole therapy in hepatic hydatidosis: a prospective randomised study. Gastroenterology 1993; 104: 1452-9.

PRIMARY ADENOCARCINOMA OF THE SMALL BOWEL

Anil K.Kaul; Vuthaluru Seenu; Omhirsch Coshic; Narasimha Mohan; Arvind Kumar; Sanjay Thulkar; Anurag Srivastava.

Abstract: *Three cases of primary adenocarcinoma of jejunum are presented. The rarity of the tumour and the vague symptomatology on presentation in all the three cases resulted in problems in arriving at a correct preoperative diagnosis. Review of literature revealed similar dificulties in earlier reports and highlighted the need for a high index of suspicion and use of appropriate diagnostic techniques to make an early diagnosis to improve the overall outcome of this disease.*

Key words: *Adenocarcinoma, Jejunum, Ileum, Small bowel neoplasms.*

JK-Practitioner 1999; 6(4):310-313

Introduction:

Though the small bowel forms two-third of the length and nine-tenths of the mucosal surface of the gastrointestinal tract, it harbours only 1-2% of all gastrointestinal malignancies. As there are no specific signs and symptoms associated with these tumors, they come to notice only when far too advanced for a favourable outcome. Prognosis can be improved by early detection when curative treatment is possible. A high index of suspicion is required in cases with vague abdominal symptoms especially those with evidence of gastrointestinal bleeding and yet having normal upper and lower GI studies. The use of imaging techniques like double contrast small bowel enema (enteroclysis) and the use of small bowel endoscopy may lead to a better outlook for these patients. The aim of this study is to highlight the need for early detection of these cases.

Case Reports

Case I

A 35 year old farmer was admitted with 5 month history of poorly localized pain in the abdomen associated with dyspepsia, occasional vomiting, loss of appetite and significant loss of weight. He had noticed a gradually progressive lump in the abdomen 2 months prior to presentation and was having progressive constipation for 1 month.

Examination revealed marked pallor. There was no significant lymphadenopathy. Abdominal examination revealed a non tender, 10 x 8 cm firm lump withnodular surface and well defined margins in the left hypochondrium extending to the epigastrium and umbilical regions, which moved with respiration, was firm in consistency, had a nodular surface and well defined margins.His haemoglobin was 3.2% with occult blood in stool. Serum biochemistry and chest X-ray were within normal limits. His barium enema revealed an obstruction at the splenic flexure with shouldering-suggestive of malignancy. Barium meal follow through did not reveal any mucosal abnormality though the bowel loops were displaced around the lump. Abdominal ultrasound could not characterize the anatomical origin of the lump. There were no secondaries in the liver. On colonoscopy luminal narrowing was detected just beyond the splenic flexure which was not negotiable. However there was no mucosal abnormality. A provisional diagnosis of carcinoma colon involving the splenic flexure was made. The patient was prepared for surgery with pre-operative blood transfusion, and mechanical as well as chemical bowel preparation. At surgery a 15 x 10 cm exophytic growth was seen arising from the proximal jejunum and infiltrating the transverse colon. There were enlarged nodes in the adjacent mesentery. No ascitis, liver secondaries, peritoneal deposits or paraortic nodes were seen. A jejunal resection with 'enbloc' transverse colectomy was performed encompassing the enlarged mesenteric nodes with a duodeno-jejunal and colo-colic anastomosis. The patient made an uneventful recovery. On cutting open the resected specimen, an ulcero-proliferative growth involving all layers of the jejunum with mucosal ulceration was seen. The muscular wall of the transverse colon was infiltrated, but the mucosa was intact. Histopatholohy revealed an adenocarcinoma of the jejunum with transmural invasion. Dissected lymph nodes showed tumour deposits. In view of the advanced

From the Department of Surgical Disciplines & Radiodiagnosis, (Kaul, Seenu, Coshic, Mohan, Kumar, Thulkar, Srivastava) AIIMS New Delhi (India)

Received July 1999 . Accepted September 1999

Correspondence to :Dr. V.Seenu. Assitant Professor Deptt. of Surgical Disciplines AIIMS, New Delhi, India.

nature of the lesion, he was given adjuvant chemotherapy with weekly injections of 5-Fluorouracil and oral Levamisole for one year. He has been on follow-up for nine months since completing adjuvant therapy and has no evidence of disease.

Case 2

A 57 year old farmer was admitted with chief complaints of a gradually progressive lump in the central abdomen of 5 months duration with loss of appetite, loss of weight, and passage of altered blood per rectum. He had a past history of occasional abdominal discomfort and dyspepsia. There was no history of altered bowel habits.

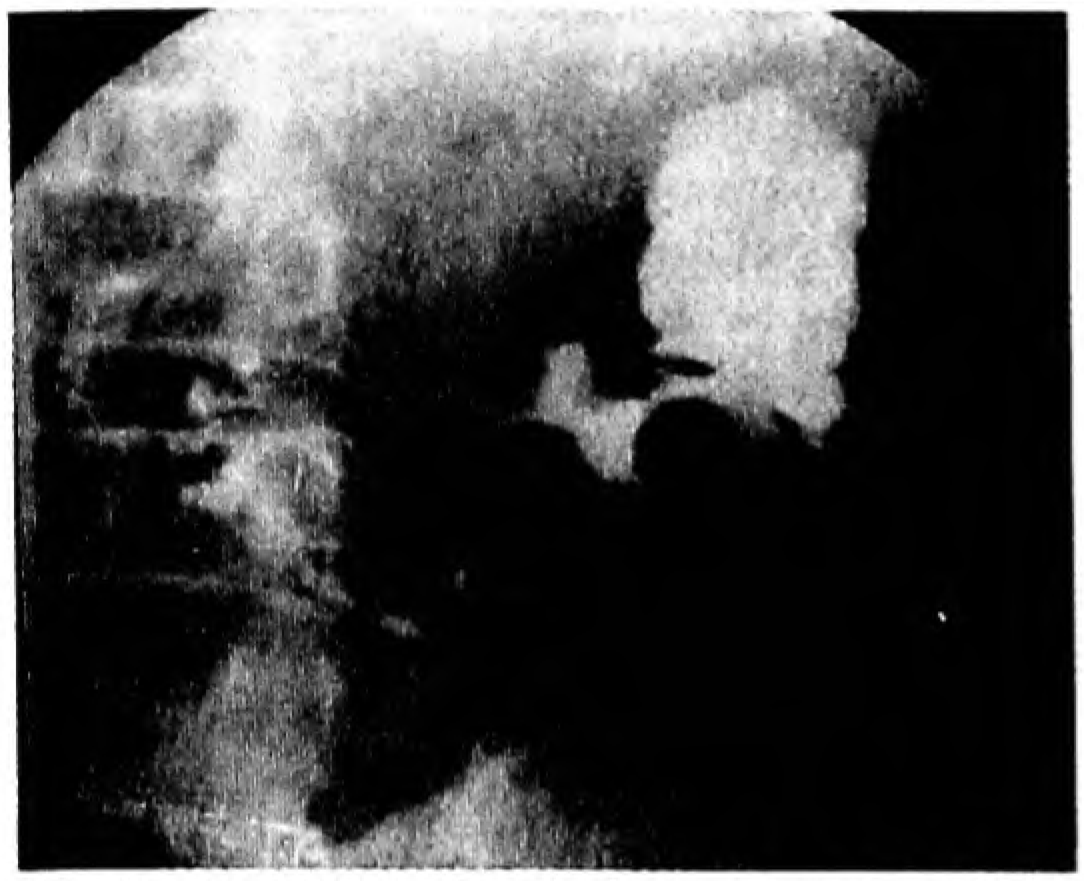


Fig. I Barium meal follow through shows abrupt, irregular and accentric narrowing of jejunal segment suggestive of a malignant stricture-a small ulcer is also seen

On examination, he had pallor and evidence of recent weight loss. There was no significant lymphadenopathy. Abdominal examination revealed an irregular lump, 18 x14 cm in size, occupying the umbilical region and extending to the epigastrium and left hypochondrium. The lump was non tender, firm and mobile. Investigation revealed a Hb of 5.7 gm%, normal liver function tests, and normal Chest X-ray. Stool was positive for occult blood. Barium enema revealed an extrinsic compression on the transverse and decending colon. Barium meal follow through suggested a mass in relation to the jejunum,distal to the duodeno-jejunal flexure (Fig.I). An ultrasound guided biopsy of the abdominal lump showed fragment of glands with marked pleomorphism. A provisional diagnosis of small bowel tumour possibly a leiomyosarcoma arising from the jejunum was made. The patient was taken up for surgery after pre-op blood transfusions and bowel preparation. At laparatomy, a large ulceroproliferative growth arising from the proximal jejunum with a predominant exophytic component was found. Adjacent lymph nodes were enlarged. Resection with a wide margin including the involved mesentery encompassing all enlarged lymph nodes was performed with an end to end jejuno-jejunal anastamosis. Histopathology revealed an adenocarcinoma of the jejunum. The lymph nodes were dfree of tumour. The patient had an uneventful postoperative recovery. He was well for about 1 year when he developed a vague pain in the upper abdomen which was followed by the appearance of a lump to the right of the midline vertical scar. An abdominal wall recurrence was suspected. CECT scan showed a tumor in the anterior abdominal wall with extension to adjacent bowel loops (Fig. II). There was no evidence of disease in the rest of the abdomen. FNAC from the lump revealed an adenocarcinoma. His metastatic workup revealed no evidence of disease elsewhere. He was taken up for surgery again. At surgery, he was found to have a second tumor in the mid ileum far away from the previous resected site. There were no significant lymph nodes. The previous anastomosis was normal. The tumor had invaded the anterior abdominal wall which was resected 'en bloc' with the mid ileum and its adjacent mesentery. There was no polyp felt or seen in the rest of the small bowel. Histopathology revealed an adenocarcinoma of the proximal mid-ileum, infiltrating upto the serosa but the abdominal wall was not involved. The patient made an uneventful recovery. After discharge, he was advised adjuvant chemotherapy with 5-Fluorouracil, Adriamycin, Mitomycin an Levamisole. He has been on follow up for six months and is at present free of disease.

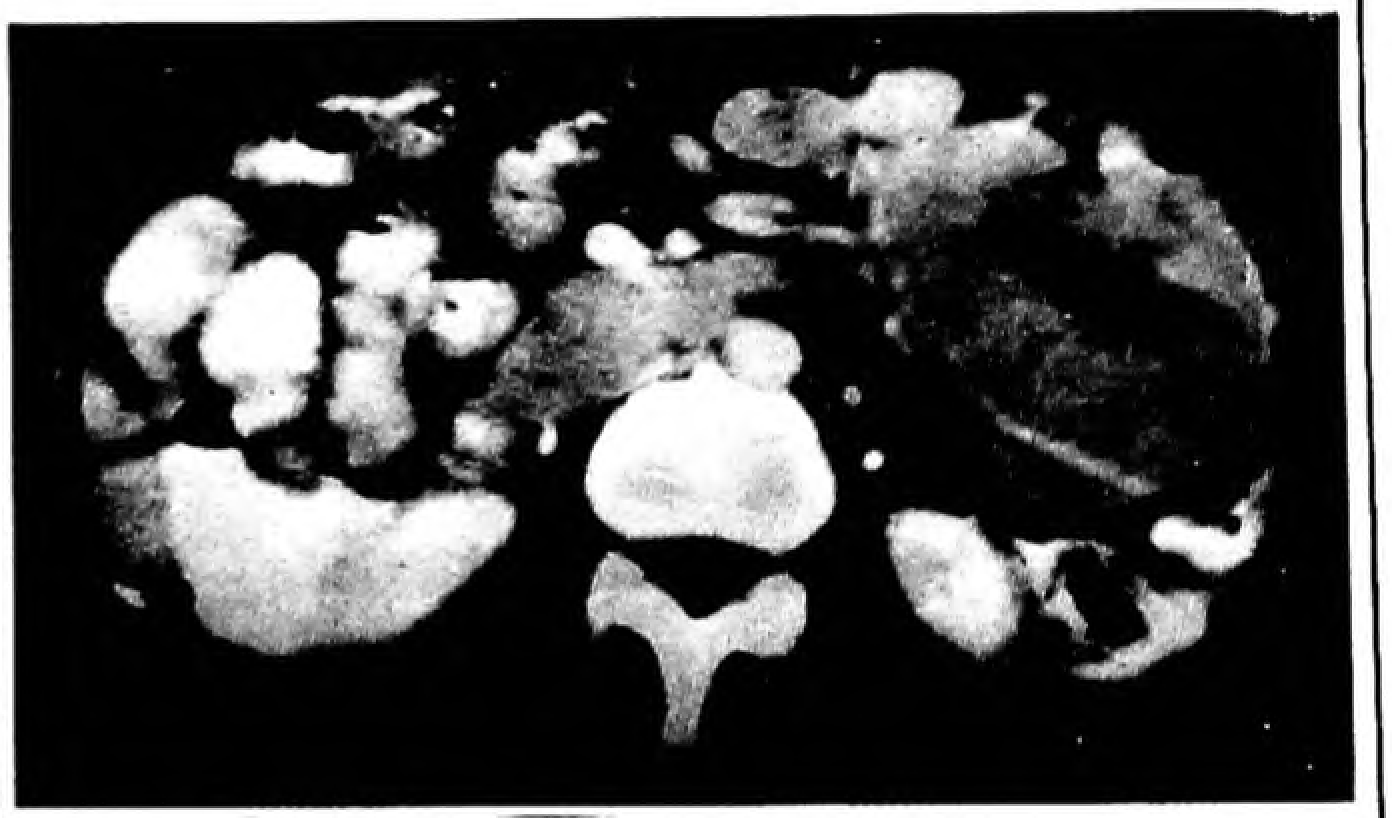


Fig. II GECT abdomen shows irregular, bulky wall thickening of a small bowel segment which shows significant enhancement suggestive of a intramural lesion.

Case 3

A 45 year old housewife was admitted with a 8 months history of heaviness in the abdomen. She had noticed a lump in the right part of her abdomen one month prior to admission. The lump had gradually grown in size since then; however she had no pain or any obstructive symptoms. She had lost her appetite as well as weight. She had two episodes of malena three years ago for which she had not been investigated.

General physical examination was normal except for pallor. Abdominal examination revealed a 12x14 cm. firm globular lump in the epigastrium extending into the right hypochondrium and umbilical region. It had restricted mobility a smooth surface and well defined margins. Investigations showed a haemoglobin of 9gm/dl. X-ray chest and serum biochemistry were normal. Ultrasonography demonstrated a subhepatic, solid mass. It was reported to be of bowel origin. Barium meal follow through showed a mass lesion compressing upon the jejunal loops; no obstruction or intra luminal lesion was seen. CT scan revealed a right sided intra-abdominal mass with lymph nodes at the base of the mesentery (Fig.III). The mass had a necrotic centre with air inside it. The patient was prepared for surgery and a laparotomy performed under general anaesthesia. At operation a large mass was seen arising from the proximal jejunumand extending into the adjacent mesentery. The tumor was extending upto the base of the mesentery and was reaching the superior mesenteric vessels. In addition loops of ileum were also stuck to the tumor. Multiple nodes in the mesentery were enlarged. In view of the vascular involvement of the lesion the tumor was considered inoperable. Biopsies were taken and the abdomen was closed. Histopathology revealed an adenocarcinoma. Prognosis was explained to the patient and her relatives. Chemotherapy was offered, but the patient refused it. She was subsequently lost to follow-up.

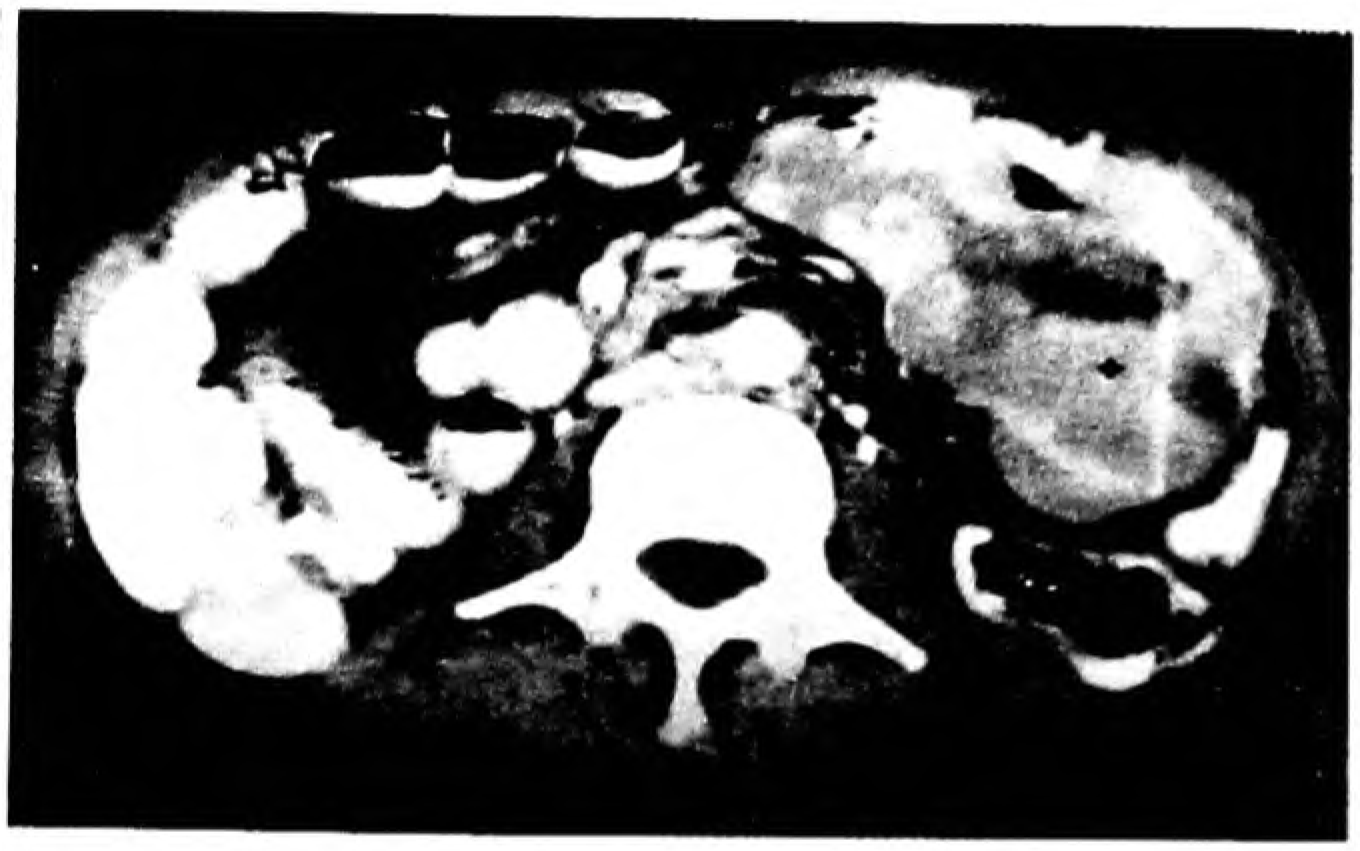


Fig. III CECT abdomen shows a similar (as in Fig II) but large intramural mass lesion with enhancement suggestive of a intramural mass lesion

Discussion

Despite constituting two-thirds of the length of the gastro-intestinal tract, the small bowel harbours only 1-2% of all gastrointestinal malignancies. This low incidence of tumors of the small bowel is due to the rapid transit time of small bowel contents, their fluid nature and relative sterility, rapid proliferation of small gut mucosa, presence of the mucosal enzyme benzpyrene hydroxylase and high levels of IgA in the small bowel mucosa[1]. Adenocarcinoma is reported to be the commonest malignant tumor of the small bowel in most series[1,2], although some mention lymphoma to be the commonest[3,4]. Adenocarcinoma is distributed equally in the duodenum and jejunum (41.3%, 43.4% respectively) with ileum being an uncommon site (15.1%)[5]. Adenocarcinoma can occur 'de novo' or arise from premalignant conditions like polyps (solitary or a part of familial adenomatous polyposis or Peutz Jeghers syndrome) and Crohn's enteritis[2]. Celiac sprue may also lead to adenocarcinoma[1]. Malignancy has also been known to arise with higher frequency in ileal conduits and in Brooke ileostomy[2]. Upto a fourth of cases may harboour associated malignancies elsewhere[2]. These are mainly gastro-intestinal, which can be synchronous or metachronous. Case no. 2 in our report had a metachronous adenocarcinoma of the ileum. Others like endometrial, breast, prostatic, vesical, ureteral, oropharyngeal and basal cell malignancies have also been reported[2]. These patients are also known to have a high incidence of non-malignant GI diseases like peptic ulcer disease and gall stones[2]. This make early dignosis even more difficult. Symptoms caused by small bowel tumours are vague or non-specific. Pain abdomen, though the commonest presenting feature is usually non-specific and not easily localized. Dyspepsia is a prominent feature in most patients. About 30% of patients have weight loss and about 25% present with anemia and gross or occult GI bleeding[2]. The patients may also present in the emergency room with obstruction[2].

Perforation as a presenting feature of adenocarcinoma is rare[2]. At diagnosis the duration of symptoms range from 1 month to 1 year, with a mean duration of 8 months[3]. In our patients the mean duration of symptoms was six months. Signs are absent in early stages. later on, anemia may be a prominent feature. An abdominal mass is palpable in upto 30% of patients, and usually signifies advanced disease, as was encountered in all the three of our patients. Radionucleide scans and angiography may localize bleeding tumours. Ultrasound and CT Scan are not very helpful for diagnosis, but are useful for staging. Double contrast small bowel enema has a sensitivity of upto 95% and is at present highly recommended[3]. Another diagnostic modality of promise is enteroscopy. Push enteroscopy can visualize small bowel upto 60 cm. distal to the DJ flexure[1]. Sonde enteroscopy can visualize the entire small gut but is time consuming, uncomfortable for the patient, needs specialized skill to perform and does not have channel for biopsy. However the pickup rate with this technique is the best reported so far.[1] Despite investigations, diagnosis is most often elusive. Desa et al have found that a correct preoperative diagnosis could be made in only 31% of patients with jejunal tumours. They however did not use enteroclysis or enteroscopy.

Treatment is by surgical excision with adequate margins, including the associated mesentery with its draining lymph nodes. If the tumor has invaded contiguous structures, 'en bloc' resection is advocated and most often possible. If resection is not possible a 'by-pass' operation should be carried out for palliation. The outcme is determined mainly by tumor stage. Nodal metastasis decreases 5 year survival from 70% to 13%[1,2]. Location of the tumor also affects prognosis. Jejunal tumors show better 5 year survival(46%) compared to duodenal (25%) and ileal (20%) tumors. Overall survival is about 30%[5]. Stage for stage, the prognosis of adenocarcinoma of the small bowel parallels that for adenocarcinoma of the colon[2].

In summary, adenocarcinoma of small bowel is uncommon. It has a poor outcome because of late presentation and delay in diagnosis. If detected and treated early, outlook for these patients will improve significantly. This needs a high index of suspicion in patients with vague abdominal pain and non-localizable source of gastrointestinal bleeding. Aggressive and more frequent use of investigations including enteroclysis and small bowel endoscopy in these patients, may help in early diagnosis and improve the outcome.

References:

1. Stone J. Small bowel malignancies. In Clinical Oncology: Churchill Livingstone; 1995; pp 1945-63.
2. Ouriel K, Adams JT. Adenocarcinoma of the small intestine. Am. J Surg 1984;147:66-71.
3. Zoolinger RM., Sternfeld WC., Schreiber H. Primary neoplasms of the small intestine. Am. J Srug 1986;151:654-58.
4. Desa LAJ, Bridger J., Grace PA., Krausz T. and Spencer J. Primary Jejuno-ileal tumours. A review of 45 cases. World J Surg 1991;15:81-87.
5. Zucchetti F., Bellantone R., Frontera D., Crucitti A., Bilanzone M., Crucitti F., Adenocare inoma of the lsmall intestine. Int. Surg 1991;76:230-34.
6. Freund H., Lavi A., Pfefferman R., Durst A. Primary neoplasms of the small bowel Am. J Surg 1978;135:75-59.

BRONCHIAL CARCINOID — A DIAGNOSIS ON FIBREOPTIC BRONCHOSCOPY

G.Q. Khan M.D.; G.Mohi-u-Din M.D.; G. Hassan M.B.B.S.; M. Yaseen M.D.; T. Masood M.D.; A.R. Khan M.D.

***Abstract:** Carcinoid tumour is a benign lung neoplasm representing 1-5% of all lung tumours, and can also occur in most organs of the body. These are derivatives of Kulchitsky cells with typical histophathology feature. A case diagnosed during fiberoptic bronchoscopy is described.*

***Key words:** Carcinoid tumour, Fiberoptic bronchoscopy.*

JK-Practitioner 1999; 6(4):314-315

Case Report:

A 26 year non-smoker male was admitted with history of massive baemoptysis, clinical examination was normal. Laboratory investigations revealed Hb. 8.5 gm/dl, TLC 11000/mm^3, DLC ^{P}72, ^{I}26, ^{F}02 (%)^{RT}, BT-20", CT 5'-15", platelet count 1.5 lakhs/mm^3 and ESR 50mm/IHR. Sputum was negative for AFB and malignant cells.

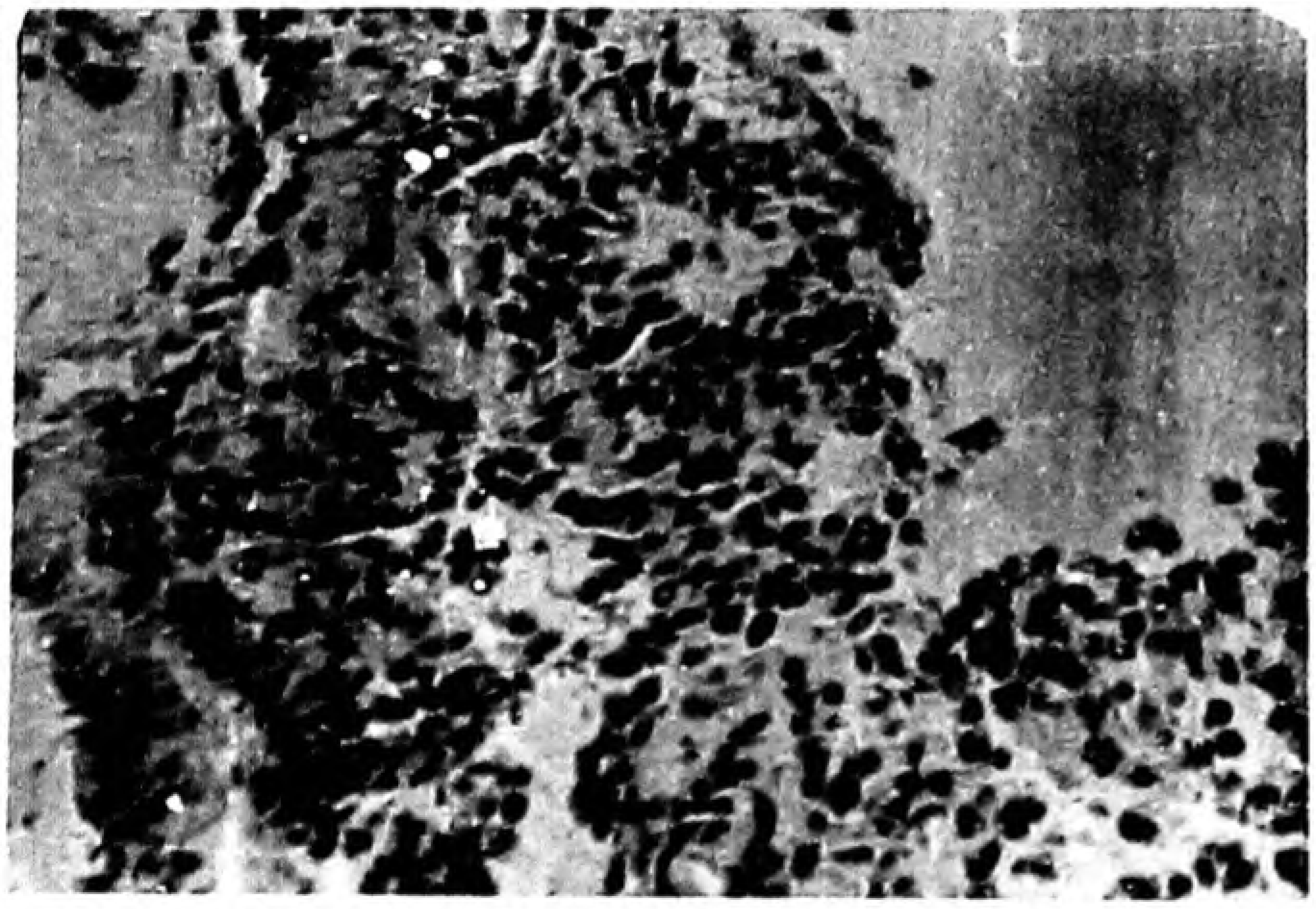


Fig. I Histopathology of carcinoid Bronchus showing montonous small tumor cells (HXEX200)

Ultrasonographic examination of the abdomen was normal. The patient's chest radiography revealed a more or less oval opacity (3.0x3.5cm) in right midzone. On fibreoptic bronchoscopy there was a cherry red tumour covered with intact epithelium in the lateral segment of right middle lobe. A biopsy was taken, and, histopathological examination of the tissue obtained showed microscopic features of carcinoid tumour (Fig.I).

Histologically the tumour was found to be composed of small round tumour cells monotonously similar to each other and characterised by pale pink cytoplasm, with round to oval nucleus and stippled chromatin; no cyto logical atypia, and mitotic activity. The tumour cells were arranged in nests and cords separated by delicate fibrous stroma. The tumour also showed areas of increased vascularity and fibrous tissue septa. The patient was subjected to surgery and a right middle lobectomy was done 2 months aftér the diagnosis was made. The operative findings were that there was a mass in right middle lobe which was of the size of 3x3.5 cm and not extending outside the lung.

Discussion

Carcinoid tumour of the lung is a benign lung neoplasm[1]. Bronchial carcinoids represent 1.5% of all lung tumours[2,5]. Carcinoid tumours occur in most organs of the body[6]. The foundation for the present day concept of carcinoid tumour was established whenMasson demonstrated that appendiceal carcinoids were a proliferation of Kulchitsky cells[7]. Most of the patients with carcinoid tumours are under 40 years of age and the incidence is equal for both sexes. There is no known relationship to smoking or other environmental factors[4]. Patients may present with chronic cough, recurrent haemoptysis, or obstruction with atelectasis, lobar collapse, or pneumonitis and abscess formation. It is derived from the normal bronchial epithelial compnents, the Kulclitsky cell[1,4]. Not only carcinoid tumours but also all types of bronchial adenomas, because oof their endobroncial and often central location, are usually visible via fibreoptic bronchoscope and hence tissue for

From the Department of Medicine (Prof Khan, Mohi-ud-Din, Hassan Yaseen, Masood) **and Pathology** (Prof. Khan), **Govt Medical College Srinagar, India.**

Received April 1999 Accepted September 1999

Correspondence to : Prof. G.Q. Khan, 3-School Enclave, Rawalpora P.O.Sanat-Nagar, Srinagar, Kashmir, India.

histological diagnosis is obtained in this manner[1]. Because carcinoid tumors are hypervascular they can bleed profusely after bronchoscopic biopsy[1,5]. Carcinoids can be locally invasive or recurrent[1], are potentially malignant[8-12] and can metastasize[1,]. Bronchial epithelium is not usually ulcerated which is the reason that tumour cells from bronchial carcinoids are usually not present in the sputum or in the bronchial secretions. These tumours can not be removed completely by marsupialization through the bronchoscope[5]. They rarely exceed 3-4 cm in diameter[4]. Carcinoid tumours usually arise from a main stem bronchus[4,14] or segmental bronchus and can often be seen bronchoscopically as an intraluminal tumour generally covered with intact epithelium[1,4].

Histologically the tumour is composed of nests, cords and masses of cells separated by a delicate fibrous stroma. The individual cells are quite regular and have uniform round nuclei and infrequent mitoses. Occassionally they display variation in size and shape of cells and nuclei, thereby exhibiting pleomorphism[4]. Surgical excision is the primary treatment of all types of bronchial adenomas, with five year survival rates of 95%, decreasing to 70%if regional nodes are involved. Effective treatment of carcinoid may require more than one approach. The symptoms like diarrhoea, wheezing may require symptomatic relief. Methylxanthine bronchodilators and glucocorticoids are helpful in relieving the dyspnea and wheezing associated with bronchial carcinoids. Octreotride, a potent inhibitor of hormone secretin by carcinoid cells, is prescribed at dose of 150 to 1500 mg/d and is effective in management of acute, life threatening manifestations. Surgery, hepatic artery embolization and chemotherapy have been used to reduce the burden of tumour tissue, interferon alpha has been shown to reduced tumour size in 10-20%, decrease symptoms and urinary 5-HIAA in upto-two third of patients. In patients with carcinoid syndrome, median survival is 2.5 years after the first episode of flushing, and prognosis is universely related with the degree of 5-HIAA elevation[15].

References:

1. JohnD.Minna. "Neoplasms of the lung". Harrison's Principles of Internal Medicine 1994; Vol.2 13th ed. 1221-1229.
2. Sayler D.C. and Eggleston C. "Bronchial Carcinoid Tumour." Cancer 1975;36:15.
3. HURT, R and Bates M. "Carcinoid Tumor of the bronchus". Thorax 1985;39:617.
4. Ramzi S. Cotran, Vinay Kumary, Stanley, L. Robbins. "Bronchial Carcinoids." Robbins Pathological basis of Disease 1989;802-803.
5. Juan ROSAL. "Bronchial Carcinoids" Ackerman's Surgical Pathology Edition 6th, 1981; Vol1: 273-278.
6. Briselli Michael,- Mark Gene J, Grillo Hermes C."Tracheal Carcinoids". Cancer 1978;No.6,Vol. 42: 2870-2879.
7. Masson P."Carcinoid and nerve hyperplasia of the appendicular mucosa." Am. J. Pathol 1928;4:181-211.
8. Arrigoni, MG, Wollner, L.B; Bernatz, P.E; "Atypical carcinoid tumour of the lung." J. Thorac Cardiovasc Surg. 1972;64:413-421.
9. Rosai J, L, evine, G; Weber W.R.; and Higa E. "Carcinoid tumours and oat cell carcinoma of the thymus", Pathol Ann. 1976; 11:201-226.
10. Smith R.A. "Bronchial Carcinoid tumours". Thorax 1969;24:43-50.
11. Turnbull, A.D., Hovos, A.G.; Goodner, J.T.; and Beattie, E.J. Jr, "The malignant potential of bronchial adenoma". Ann. Thorac. Surg 1972;14:453-462.
12. Wisniewski, M; and Fayemi, A.O; "Bronchial Carcinoid". A malignant tumor". Chest 1972;62:760-762.
13. Grillo, H.C.; "Tracheal tumors, Rhoad's text book of surgery, 5th edition; J.D. Hardy, Ed. Philadelphia. J.B. Lippincott, 1977;1364-1371.
14. Anthony Seaton, Douglas Seaton and A. Gordon Leitch. "Bronchial Carcinoid tumor". Crofton and Douglas Respiratory diseases, 1989;984-987.
15. Lee M. Kaplan. "Endocrine tumours of the gastrointestinal tract and pancreas", Harrison's Prinicples of Internal Medicine 14th Ed. 1998;585-588.

PSEUDOTHALIDOMIDE SYNDROME IN ASSOCIATION WITH INTRA-UTERINE INFECTION

G.M. Ladakhi M.D.; M.Mubarik M.D.; N.A.Reshi M.D.; Basharat Nabi M.B.B.S.; A.S. Sethi M.D.

Abstract: *Pseudothalidomide Syndrome or Hypomelia-Hypotrichosis Syndrome is a rare autosomal recessive disorder.One such case, associated with Intra-uterine Infection (Toxoplasmosis) is presented here, the first of its kind reported from the Kashmir valley.*

Key words: *Pseudothalidomide, Hypomelia - Hypotrichosis, Autosomal recessive, Toxoplasmosis.*

JK-Practitoner 1999; 6(4):316

Case Report:

One hour old newborn male, born by normal vaginal delivery, fifth in birth order was admitted in a neonatology ward of main teaching cum referral children hospital of the valley with abnormal features on examination. The features included microcephaly, sparse hair, hypertelorism, shallow orbits, prominent eyes with bluish sclerae and icterus, low-set ears with hypoplastic lobules, cleft palate, extreme hypomelia with syndactyly of all limbs and three fingers in each hand. Abdominal examination revealed hepatomegaly. The baby had profound growth deficiency with birth weight of 1.7kgs and birth length of 30 cms.

The baby cried immediately after birth and passed urine and meconium normally. Intravenous fluids were given through umblical vein on the first day. The baby accepted bottle feeds on the second and the third days with death occurring on the fourth day.

Family history revealed previous sib deaths of the second, third and fourth issues. All the three had died with diagnosis of Pseudothalidomide Syndrome on day first, day fourth and day first of their birth respectively. However, the first issue was normal female at birth and is eleven years old at present with no abnormality. There was no history of consanguinous marriage. TORCH screening test for Toxoplasmosis (Ig^M) was positive in mother during late second trimester of previous pregnancy and was treated with spiramycin then onwards.

On investigation, haemogram revealed haemoglobin of 14 gms/dl, total leukocyte count of 12,000/dl, the differential being 80% lymphocytes and 20% polymorphs and platelet count 1.5 x 10^6/dl. Test for C-reative proteins was negative. Serum bilirubin was 12 mgs/dl, the conjugated fraction being 4.1 mgs/dl. Serum SGOT and SGPT were 250 and 300 KA Units respectively. TORCH screening test was positive for Toxoplasmosis (Ig^M). Radiography showed poorly ossified skul bones and vertebral bodies, thin spatulated ribs and extemely hypoplastic long bones. Ultrasonography abdomen showed hepatomegly.

Discussion:

Pseudothalidomide Syndrome was initially described by Roberts in 1991[1]. Most of the babies, born at term have bith length of less than 37 cms. Infants with severe deformity usually die in early neonatal period, but the survivors have marked growth retardation and severe mental deficiency. Birth length of more than 37 cms, less severe limb deformities, absence of cleft palate and presence of thin naries are associated with a better prognosis[2,3].

Around 50% of the tested individuals have premature separation of centromeric heterochromatin of many chromosomes[4].

Our case is interesting in the sense that Pseudothalidomide Syndrome was associated with intra-utreine infection (Toxoplasmosis) which is exceedingly rare and there is paucity of literature available regarding such association.

References:

1. Roberts JB: A child with double cleft of lip and palate, protrusion of intermaxillary portion of the upper jaw and imperfect development of the bones of four extremities. Ann. Surg. 1919;70:252.
2. Herrmann J. etal; A familial dysmorphogenetic syndrome of limb deformities, characeristic facial appearance and associated anomalies. The pseudothalidomide syndrome. Birth Defects 1969;5:81.
3. Grosse FR et al; Tetraphocomelia-cleft palate syndrome. Human Genetic, 1975;28:353.
4. Parry DM et al; Phocomelia Syndrome. Premature centromeric separation and congenital cranial nerveparalysis in two sisters, One with malignant melanoma. AM J Med. Genet. 1986;24:653.

From the Department of Paediatrics, Govt. Hospital for Children, Srinagar, India (Ladakhi, Mubarik, Reshi, Nabi & Prof. Sethi)

Received March 1999 Accepted July 1999

Correspondence to :Dr. A.S.Sethi M.D. Prof. & HOD Paediatrics **Govt. Hospital forChildren, Srinagar, Kashmir, India.**

HEREDITORY MULTIPLE EXOSTOSIS

Muzaffar Jan, M.D.; Wajid Ali, M.D.; B.A.. Churoo M.D.; Mushtaq Ahmad M.D.; Masood-ul-Hassan M.D.

Abstract: *Multiple cartilaginous exostosis are bony projections found near the ends of tubular bones and ribs, the vertebral bodies, the scapulas and the illiac crest. Radiologically they appear to originate at the borders of metaphysis and sometimes along the diaphysis of long bones. Inheritance is autosomal dominant with high penetrance and variable expressivity. These may undergo rapid growth during infancy but are rarely detected radiographically prior to three years of age.*

Here we report two siblings with multiple exostosis with a negative family history. This is because of sporadic mutation.

Key words: *Exostosis, Metaphysis.*

JK-Practitioner 1999; 6(4):317

Introduction

Hereditary multipl exostosis is a disorder of metaphysis, inherited as autosomal dominant character. The lesions may be solitary or multiple and are usually located in the metaphyseal areas of long bones. Often the lesions produce no symptoms but occasionally interfere with the functions of a joint, tendon or nerve compression may result.

Case Report:

A 6 year old female child born of a non consanguinous marriage was referred to the pediatric division of SKIMS with multiple bony swellings and the impression givne was of a bone tumor. There was no history of pain, tenderness; limitation of movement or of rapid progression in the size of the swelling.

On examination the child had one swelling in left scapula; one in right scapula; swelling in both radii and one swelling in tibia. Anthropometric indices were within normal limits. Other investigations revealed normal hemogram; ESR of 12 mm, calcium 8.43 mg%; Phosphorus 6.4mg% and Alkaline phosphatase of 2.77 units. Liver and renal functions were normal.

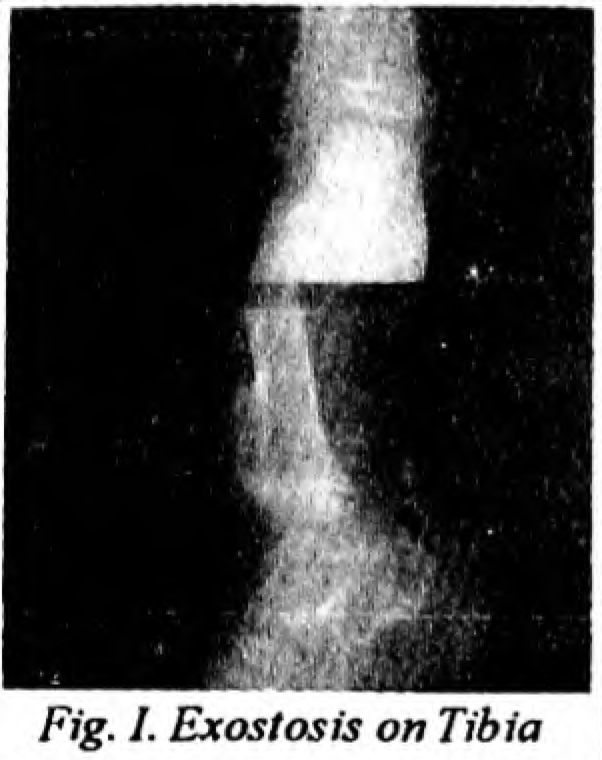


Fig. I. Exostosis on Tibia

Radiology of skelton revealed bony swellings arising from metaphysis in the areas mentioned.

Another sibling a 12 years old male child when examined had two exostosis in left scapula; one in right scapula; one in both radii and one in both tibias at upper and lower ends. Radiological examination also revealed exostosis in the said areas. There were four other siblings in the family-three female and one male. All of them were normal. Parents of the children also were normal.

Discussion:

Ethrenfried reported 12 cases in 1917 and suggested the term hereditary deforming chondro dysplasia. In 1943 Jaffee proposed the term hereditary multiple exostosis which being descriptive and simple is the most wildly used today. Diaphyseal achlasias; cartilaginous exostosis and hereditary osteochondromatosis are the titles under which the condition is reported.

Hereditary multiple exostosis is a familial condition with autosomal dominant expression. The disease also may occur sproradically due to mutations[1]. The exostosis are unsightly and disturbing to the growth of the long bones producing deformations and sometimes compression of the nervous and blood vessels[2]. The disease often does not impair stature but mild skeletal disproportion may occur because limb involvements greater than spinal involvement[3]. Malignant degeneration may occur but is very rare in childhood[4].

Cosmatically deforming or microvascular complications producing exostosis should be removed surgically. However the surgery should be deffered till growth ceases because of a high chance of regression of lesions.

References:

1. A.H. Zargar, A.I. Wani, S.R. Masoodi, Sporadic multiple exostosis. A rare cause of short stature. Journal of Medical Sciences 1998;1;28-29.
2. Krane SM; Shiller AL; Hyperostosis; Fibrous dysplasia and other disorders of bone and cartilage in Harrison principles of internal medicine (14th Edition) Mc. GTraw Hill Inc; 1998;2269-75.
3. Lee B; Identification of molecular defect in a family with spondylo epiphyseal dysplasia. Science 1989;244:979-82.
4. The skeletal dysplasias in orthopaedic disease (Physiology; Pathology; Radiology) Eds; Aegortar E; Kirk patric JA Jr. 4the edition; Saunders; Philadelphia 1987;87-200.

From the Department of Neonatology, SKIMS, Srinagar, India (Jan, Ali, Churoo, Ahmad & Prof. Hassan)

Received November 1998 Accepted May 1999

Correspondence to : Dr. Muzaffar Jan, Lecturer, Deptt. of Neonatology, SKIMS, PBNo. 27, Srinagar, Kashmir, India.

DYSCHROMATOSIS UNIVERSALIS HEREDITARIA

Qazi Masood M.D.; Iffat Hassan M.D.; Sheikh Manzoor M.D.

Abstract: *Dyschrmatosis universalis hereditaria is a rare disorder of pigmentation described mainly among Japanese and less often in other races. Here we report a case of this rare disorder in a thirteen year old Kashmiri girl who to the best of our knowledge is the first of its kind from this part of the world.*

Key words: *Dyschrmatosis universalis hereditaria; pigmentation.*

JK-Practitioner 1999; 6(4):318

Introduction

Dyschromatosis universalis hereditaria is a rare hereditable disorder of pigmentation characterized by generalized hyperpigmented macules intermingled with mottled depigmentation. The disease manifests at birth during the first few months of life and affects both sexes equally. This disorder has been described mostly among the Japanese and less often in other races.

Case Report

A thirteen year old female product of a consanguinous marriage presented to us with a history of hyper and hypo pigmentation all over body since birth, which progressed for the first twoyears of her life and then remained stationary. Family history was unremarkable except for a similar dermatolotical problem in her elder sister. Her general physical and systemic examination was within normal limits. Cutaneous examination revealed numerous hyperpigmented macules varying in sizefrom 2-3 mm present all over the body except for palms and soles. Lesions were more prominent over trunk and face was relatively spared. In addition to this, depigmented macules were also present in the midst of the hyperpigmented lesions. There was no evidence of atrophy or telangiectasis over the affected skin. Examination of halir, teeth and nails was within normal limits. The histopathological findings from hyperpigmented and depigmented macules were non-contributory.

Discussion

Dyschromatosis universalis hereditaria, the excet etiology of which is unknown, is characterized by asymptomatic pigmented macules of varying size and shapes arranged irregularly and admixed with depigmented macules. The lesions are distributed all over the body lwith the exception of plams and soles. Involvement of face is usually minimal[1-3]. Relative sparing of face and complete sparing of plams and soles was also observed in the patient under discussion.

Our patient being a product of a consanguinous marriage with her sister being afflicted similarly, seems to have inherited the disorder in an autosomal recessive fashion.

References:

1. Butterwoth T and Stream LP. Textbook of clinical genodermatology, Williams and Wilkins Co, Baltimore, 1962; pg14-15.
2. Griffiths WAD: Reticulate pigmentary disorders. Clin Exp Dermatol 1984;9:439-450.
3. Findlay GH and Whiting DA. Universal dyschromatosis. Brit J Dermatol 1971;85:66-70.

From the Department of Dermatology, STD & Leprosy GMC Srinagar, India (Masood, Iffat, Manzoor)
Received November 1998 Accepted March 1999
Correspondence to : Dr. Qazi Masood, Associate Professor & Head, Dept. of Dermatology, STD & Leprosy, GMC, Sgr.

CONGENITAL LEUKEMIA

Prof. Masood-ul-Hassan M.D.; Muzaffar Jan M.D., D.C.H.

The etiology and pathogenesis of congenital leukemia is unknown. The strongest evidence for a genetic predisposition to acute leukemia is its occurrence in identical twins. If leukemia develops in one of the twins before 6 years of age, the risk of disease in other twins is 20%. Congenital leukemia has been associated with trisomy 7, trisomy 13, Turner Sydrome and Down Syndrome[5]. In utero-exposure to carcinogens has been claimed to be responsible for some cases of Congenital leukemia.

Congenital leukemia is mostly acute myeloid type and rarely acute lymphoblastic. As per FAB classification acute myeloid is subclassified as MI (Acute myeloblastic without maturation) M2 (Acute myeleblastic with some maturation, M3 (Acute promyelocytic), M4 (Acute myeslomonocytic), M5 (Acute monecytic), M_6 (Erythroleukemia), and M_7 (Acute megakaryocytic). It is associated with higher incidence of CNS infiltration and abnormalities of the long arm of chromosomes[11]. The blast cell of congenital acute lymphoblastic leukemia (ALL) are pre-B but common Acute lymphoblastic leukemia antigen (CALL) negative. These infants have a high incidence of CNS infiltration, high leucocyte count and poor prognosis.

Cutaneous manifestation are the most frequent clinical findings noted at birth. In addition to petechae and purpura, leukemic skin nodules (i.e. leukemia cutis) have been observed in about 50% of cases. These skin nodules vary in size from a few millimeter to a few centimeters, are bluish to slaty gray in colour, may appear in all sites and are palpated as firbroma like tumors of deep skin. They may undergo spontaneous remission but tend to recur in a more generalised form within a few weeks to months. Hepatosplenomegaly is common, but is rare. Resipratory distress secondary to leukostasis within the pulmonary vasculature may occur. Other non-specific features of congenital leukemia include lethargy, pallor, poor feeding and umbilical, gastro-intestinal or genito-urinary bleeding. Leukemia like picture may occur in neonates with Down syndrome or mosaic form of this syndrome. This phenomenon has been referred to as transient myeloproliferative disorder to transient leukemia[2]. This syndrome mimics acute myeloid leukemdia. Bone marrow aspirate reveals 30% to 70% blasts, majority of which are megakaryoblasts[2]. Hepatosplenomegaly and thrombocytopenia are common findings. The hematological status of these neonates returns to normal in 1 to 4 months with only supportive therapy. Normal neonates without abnormal karyotypes in their blasts may also have spontaneous remission. The reason that spontaneous remission may occur in newborn infants with or without Down syndrome is unclear. It could be due to limited ability of committed precursor cells to proliferate or due to maturation of these cells.

Laboratory results reveal a wide range of values i.e. Hb 7-20gm/dl, Leukocyte count 2000-850,000/ mm^3 (Mean 150,000) and platelets count 6000-300,000/mm^3 (Mean - 70,000).

- The diagnosis is confirmed by examination of bone marrow aspirate obtained from the porterior iliac crest.
- Bone marrow cytogenetic analysis may show chromosomal abnormality.

Many disorders in the newborn imitate leukemia. The newborn bone marrow response to infections, hypoxemia, or severe haemolysis commonly is a leukomoid reaction and an increase in circulating nucleated erythrocytes. This is frequently confused with congenital leukemia.

Till a decade back congenital leukemia was considered fatal once diagnosed. During last 10 years there have been reports within world literature regarding spontaneous remissioin of congenital leukemia[3]. Three cases, two of which were acute monocytic and one Acute myelocytic leukemia with spontaneous remission have been documented[3]. For this purpose the present day plan of therapy in congenital leukemia is that the chemetherapy should be reserved for progressive diseases or when there is reoccurrence.

I) Initial plan of therapy should be supportive (i.e.)
   a) Double volume exchange transfusion to reduce the load of WBC which would

JK-Practitioner 1999; 6(4):319-320

From the Department of Neonatology & Critical care Pediatrics, SKIMS, Soura Srinagar, Kashmir, India (Prof. Hassan, Jan)

Received February 1999 Accepted July 1999

Correspondence to : Dr. Muzafar Jan (Lecturer), Department of Neonatology & Critical Care Pediatrics, SKIMS, Soura Srinagar, Kmr.

otherwise lead to pulmonary complication and mortality. Infact Double volume exchange should be considered as the initial therapy in congenital leukemia and should have an important place in the protocol of congenital leukemia treatment.

b) Colony stimulating factors like erythropoietin, Neutrophil stimulating and mecrophage stimulating factors and appropraite use of antibiotics if and when needed.

ii) Progressive disease and recurrence of disease is treated with chemotherapy.

Congenital AML is managed with aggressive combination chemotherapy. Double volume exchange transfusion should be considered as part of the initial treatment if the leukocyte count is greater than 100,000 cells/mm³.

- Bone marrow transplantation should be performed in first remission.
- Transfusion of cord blood containing stem cells appears promising, but needs further studies.

Congenital ALL should be managed with chemotherapy protocols used in treating childhood ALL. Cranial irradiation should be used as part of CNS prophylaxis because of the risk of damage to the developing brain. Intrathecal chemotherapy should be used instead.

Infants undergoing spontaneous remission should be followed closely for relapse. Those in whom relapse occurs appear to respond favourably to standard chemotherapy.

References:

1. Resnik Ks, Brod BE, Leukemia cutis in congenital Leukemia: Analysis and review of the World literature with report of an additional case. Arch. Dermatol 1993;129:1301-6.
2. Beatrice C lampkin, The Newborn infant with leukemia. The journal of pediatrics 1997;131-2:176-177.
3. James G. Dinules, Douglas S. Hawkins, Barbare S. Clerk, Julie S. Francis. Spontaneous remission of congenital leukemia. The journal of pediatrics 1997;131-2:300-303.
4. Isaac H. Jr. Congenital and Neonatal malignant tumors, A 28 year experience at Children Hospital of Los Angles, Am. J. Pediatr. Hematol.Oncol. 1987;9:121-129.
5. Robert J. Arcei, Howard J. Wingtein. Neoplasia, Neonatology pathophysiology and management ofd thé newborn, fourth eidition edited by Gorden B Avery, Marry Anin. Fletcher and Mhavivi G. McDonald. J.B. Lippincet Company, Philadelphia 1994;54:1211-1217.

SPINAL ARACHNOID CYST PRESENTING AS COMPRESSION PARAPARESIS

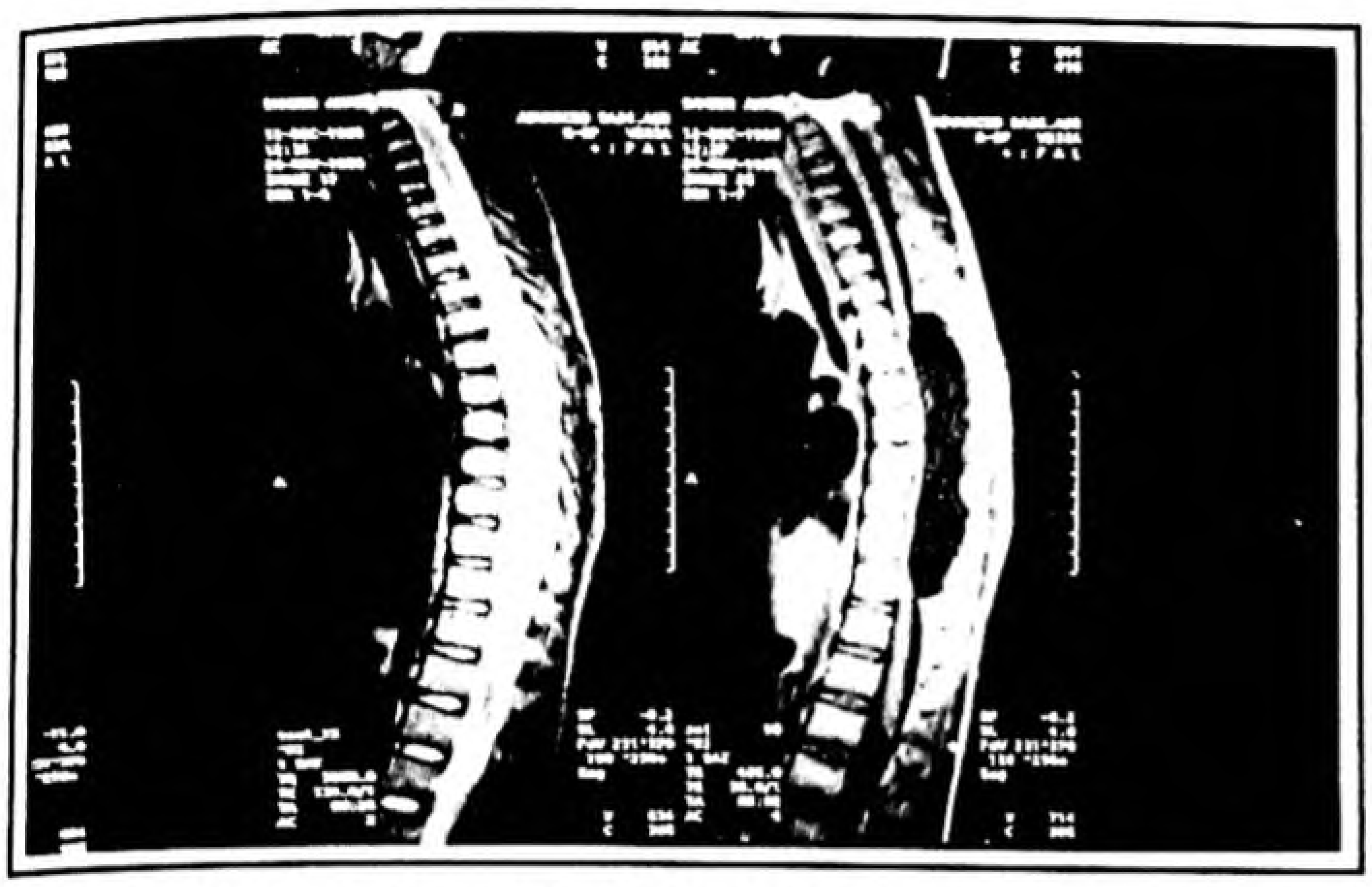


Fig.A : Wide spinal canal D4 to D11. Hypointense signal seen on T1W1 (right panel) and hypertense signal on T2W1 (left panel) causing anterior displacement of the cord with compression characteristic of arachnoid cyst.

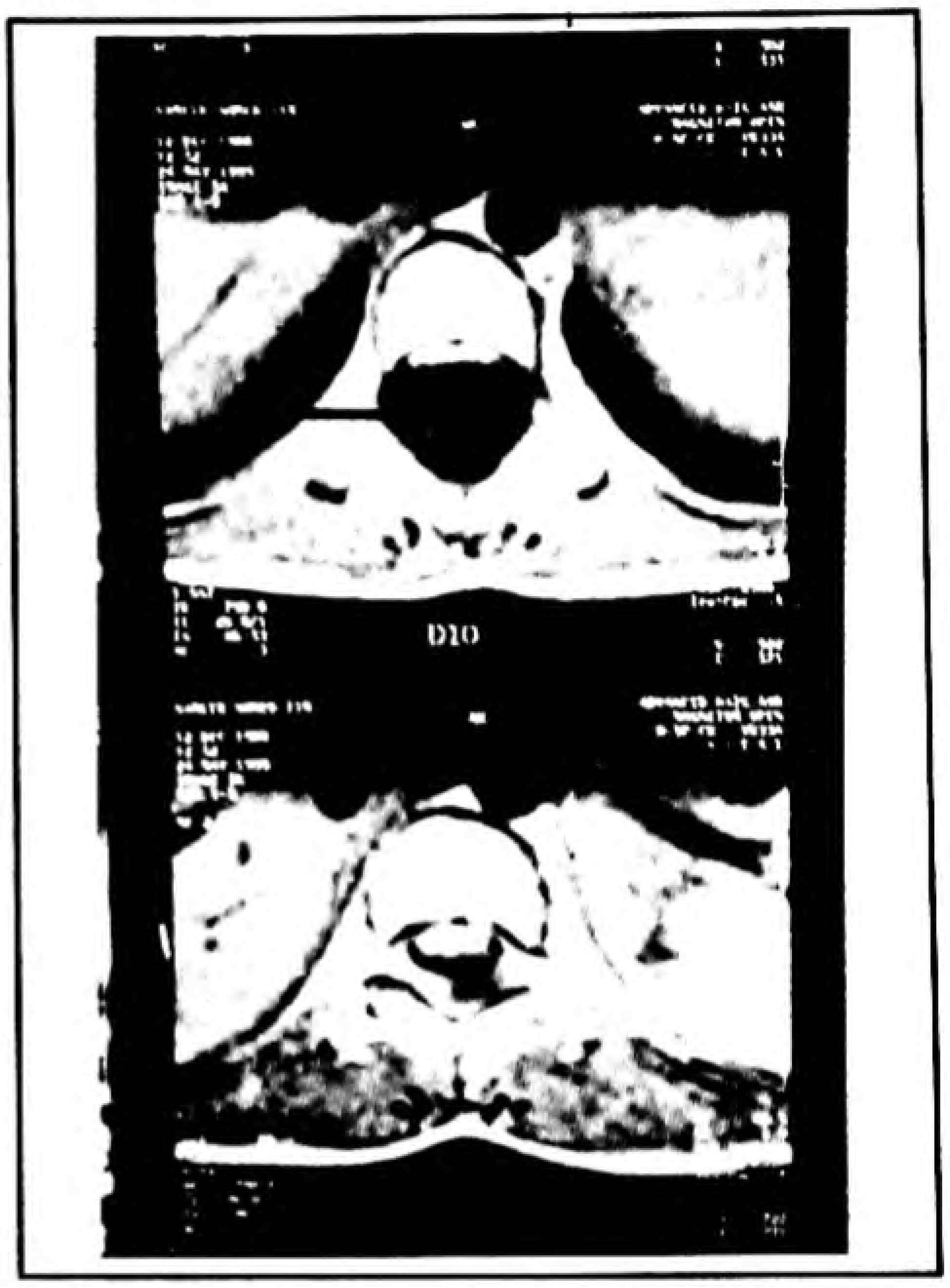


Fig.B: Hypointense signal seen on T1W1 with thinning of the cord (see arrow)

An eleven year old boy, from a rural background, with an uneventful birth history and normal mental and motor milestones, fully immunized presented with four months history of progressive stiffness of lower limbs associated with difficulty in walking without any sensory complaints. There was no bowel or bladder involvement. Patient denied any history of headache or trauma. Clinical examination revealed spastic parapaesis, scissor gait, absent abdominal reflexes, bilateral Babinski's positive, and decreased sensations for pain and touch below D6. Lower dorsal spine revealed Smooth, non tender kyphosis. MRI of dorsal spinal revealed widening of spinal canal from D4 to D11 level with a mass seen posteriorly with increased signal on T2WI, and a hypointense signal on T1WI imaging, causinganterior displacement of cord along with compression at these levels. (See figure A and B). Patient was evaluated for a possibility of congenital or hydatid cyst of spinal arachnoid space. Serology for hydatid disease was suggestive. Ultrasound abdomen and chest radiography were normal. Patient wa shifted to neurosurgical unit for further management.

From:
S.M. Saleem M.D., DM.; *M. Hayat* M.D.
G.N. Dhobi M.D. *Sonaullah Shah* M.D.
Department of Internal Medicine
SKIMS, Soura, Srinagar India
JK-Practitioner 1999;6(4):321

RADIATION SAFETY STATUS IN NUCLEAR MEDICINE DEPARTMENT OF SHER-I-KASHMIR INSTITUTE OF MEDICAL SCIENCE, SOURA, SRINAGAR

M.A. Bhat; A.G. Sofi; S.K. Kaul.

Abstract: *There are 145 radiation workers in the Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir. Among these radiation workers 25 are working in the department of Nuclear Medicine. These radiation workers are involved in various procedures using unseated radio isotopes. Presented in this study is the personnel exposure of these radiation workers from 1982 to 1990 received during various procedures.*

It has been observed that the average radiation levels of these occupational workers on nuclear Medicine department are 151.19mR/yr; 2090.71mR/Yr;318.44mR/yr and 145. mr/yr as regards to doctors, technologists, research fellows and attendants respectively. While average radiation levels of medical physics staff are: 75mR/yr. 368.8mR/yr; 154.54 mR/yr and 145.0 mR/yr respectively, which are well within permissible levels.

Key words: *Radiation, safety.*

JK-Practitioner 1999;6(4): 322-325

Introduction

Man has always been exposed to "ionising radiation" from cosmic rays and from naturally occurring radionuclides in soil, air, water and food. With the technological development of "Atomic Energy Programme' a new branch of medicine known as "Nuclear Medicine" has been established where various types of radiopharmaceuticals are used quite emperically as aid for diagnosis and treatment of various diseases. Extreme care is taken to ensure radiation safety in all these applications of nuclear technology by a regulatory programme which encompasses availability of trained personnel, properly designed installations with engineered safety features, and adoption of safe operating procedures.

The department of Nuclear Medicine was established at SKIMS in 1982 and is fully operational. This department was planned in consultation with BARC to restrict the exposure to the radiation workers and to the public (ALARA concept). The radioisotope laboratory as shown in layout fig.1 is designed so to have easy access good ventilation and smooth surface which can be easily washed and decontaminated if necessary. Further with the increasing use of radioisotopes at our centre for diagnosis and therapy and during the various radioisotope procedures like, separation, purification, solvent leaching, membrane filtration and formation of the radio-pharmaceuticals a need was felt to protect radiation workers and the general public from the unnecessary radiations as these operations could give rise to personnel radiation exposure[1]. To overcome these exposure levels necessary measures were taken to attenuate and to minimize the radiations. This was achieved to adopt in judicious combinations of "TIME", *"DISTANCE"* and *"SHIELDING"*[2].

The personnel dose or the dose received by an individual was taken as the whole body dose which was felt useful for an approximation and was expressed in millirems (mrem) as suggested by Atomic Energy Regulatory Board (AERB); AERB safety code SC/MED-2.

The range of isotopes used at our center, includes almost 90% of Tc-99m (Mo-99) (Technetium-99m) having average activity of 400 mCi. The rest of the 10% includes Iodine-131 Cr-51 and besides these radioisotopes P-32 having activity of 3mCi is also used for therapy as and when required. Discussed in this paper is the study of radiation exposure to the radiation workers at our centre from 1982 to 1990. The results have been drawn from our observations recorded and maintained for the above period, the observations have also been made with regard to the maximum dose received by an individual and category of personnel with reasons for its explanation. Further in addition to the personnel dose received during the radioisotope procedure is "HOT LAB", the area monitoring is also discussed separately.

From the Department of Medical Physics and Bioengineering SKIMS, Srinagar, India (Bhat, Sofi, Prof Kaul)

Received November 1998 **Accepted July 1999**

Correspondence to : Dr. S.K. Kaul, Prof. & Head, Medical Physics & bioengineering Department, SKIMS Soura, Srinagar Post Bag No. 27 India.

Material and Methods

The institute has 145 regular radiation workers in various departments. The whole body dose of these personnel was studied in a reference group of 24 employees of the Department of Nuclear Medicine at Sher-i-Kashmir Institute of Medical Sciences, who were occupationally exposed to unsealed radioisotopes. The cumulative radiation dose per year received by these personnel was measured for eight years. The personnel dose was monitored using chest and wrist film badges supplied to each individual and evaluated monthly at DRP, BARC. The up-to-date records of all personnel radiation exposure, and area monitoring data were maintained properly by the "Radiation Safety Laboratory" under the supervision of "Radiation Safety Officer"

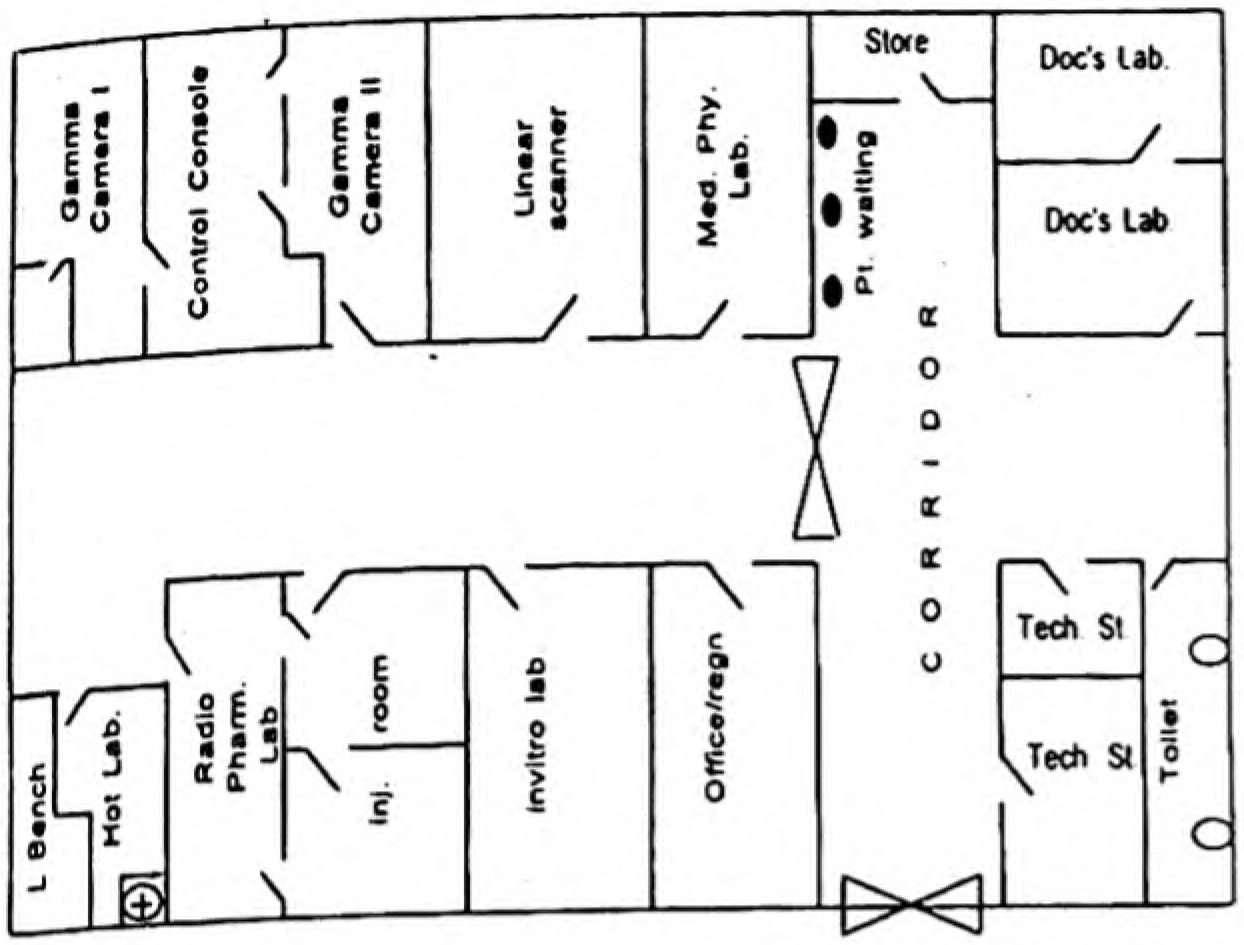


Fig. 1. Layout of Department of Nuclear Medicine SKIMS

The "Radioisotope Laboratory" of Nuclear Medicine Department was divided into following regions for radiation safety purpose.

1. Radiologically clean area-consisting of office, registration counter, doctors room and medical physics laboratory.
2. Area of manipulation of radiochemical-comprising of sample preparation room, injection room.
3. Radiologically dirty area - waste stores, incinerator, decontamination area and waste disposal site.
4. Experiment area-Diagnosis rooms (Gamma Camera room), Invivo room, thyroid uptake room etc.
5. Patient waiting area - separate for patients who have received radioisotopes.

The area monitoring was performed in the radioisotope lab. at selected different locations to better understand the radiation levels in Nuclear Medicine Department. The measurements were carried out using the below mentioned instruments.

1. Minimonitor TM-II Model 05-571 victoreen.
2. PRIMA Tm-7 Model 05-582 Victoreen.
3. 4-Decade GM Survey Meter Model 498 Victoreen.

Results and Discussion

All the radiation workers of the institute are covered by the personnel monitoring programme of division of Radiological Protection. BARC, Bombay. From the radiation protection point of view, it is obligatory for us to know exactly the radiation dose which different group of radiation workers are receiving. The personnel working in Nuclear Medicine Department are classified into four broad categories according to their nature of work. These categories are:

a. Supervisory staff (Doctors/Physicists)
b. Technical Staff (Technologists)
c. Helping staff (Attendants)
d. Others (Research fellows)

Fig. 2 represents the average whole body dose per year expressed in millirem (mrem) of the above mentioned categories. It shows the category "B" has received more dose which is expected for their nature of work. As all the technologists belonging to this group doing radiopharmacy procedure like, separation, purification and elution in a "Radioisotope Hot Lab", and are therefore exposed to increased level of radiation. The personnel belonging to category "C" has also considerably received increased level but they have received only 87.93% of dose compared to category "B" However one person belonging to category "C" has received a higher radiation dose at an average of 98.00 mrem per year although within the permissible limits. The person involved was holding the charge of washing of glass wares and cleaning of the area where activity is handled. Further the personnel belonging to the cagetories. "A" and "D" have received 41.61% and 40.04% of radiation dose respectively compared to group "B".

As the Medical Physics and Bio-engineering (M.P. & B.E.) Department of SKIMS is also involved in playing a role in functioning of the nuclear medicine department. Fig.3 depicts the personnel dose distribution per year of this department and the nuclear medicine for various categories of workers. It has been observed that the radiation workers of nuclear medicine department from category "A" received 59.20% more dose than personnel of the same category of M.P. & B.E. Department. This is due to the fact that the nuclear medicine staff of this

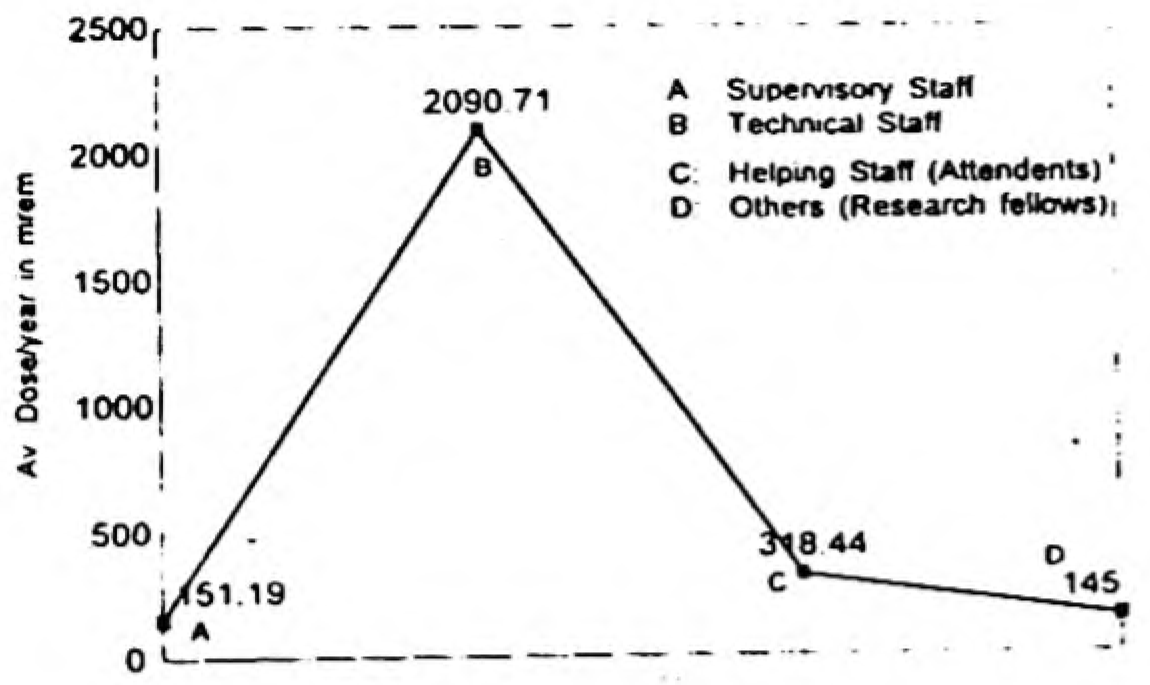


Fig.2: Personnel Category

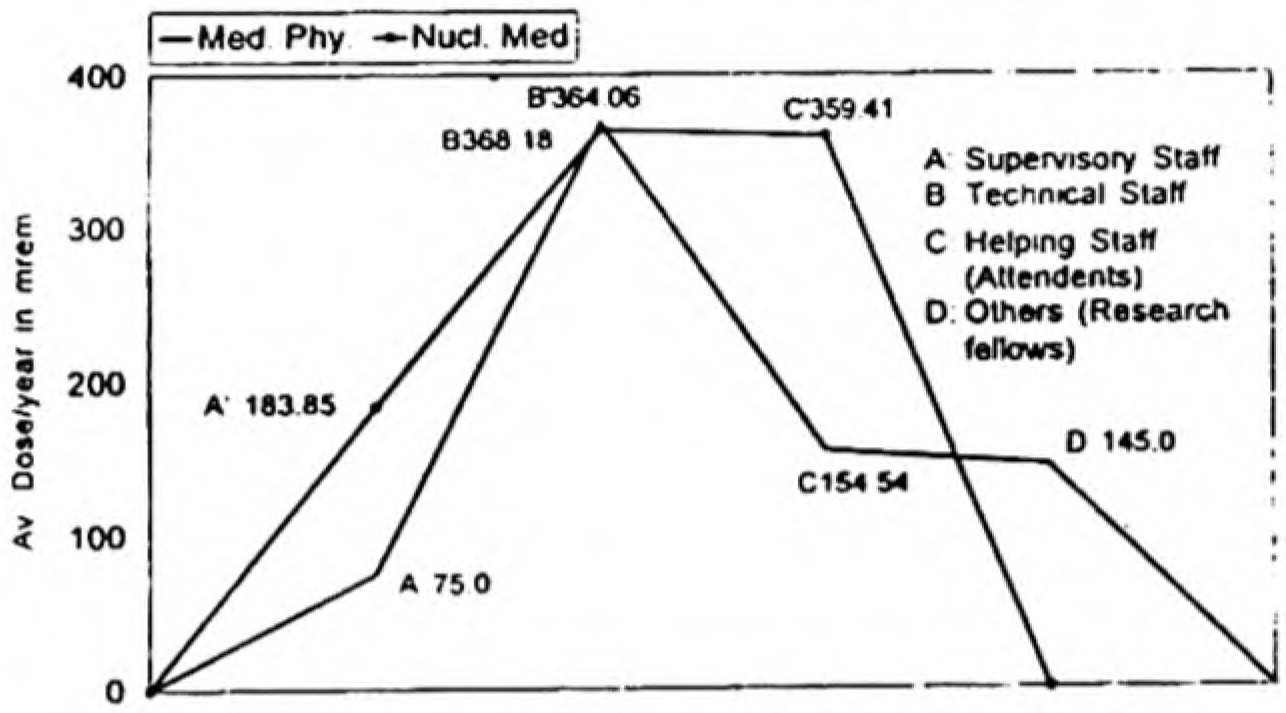


Fig.3: Personnel Category

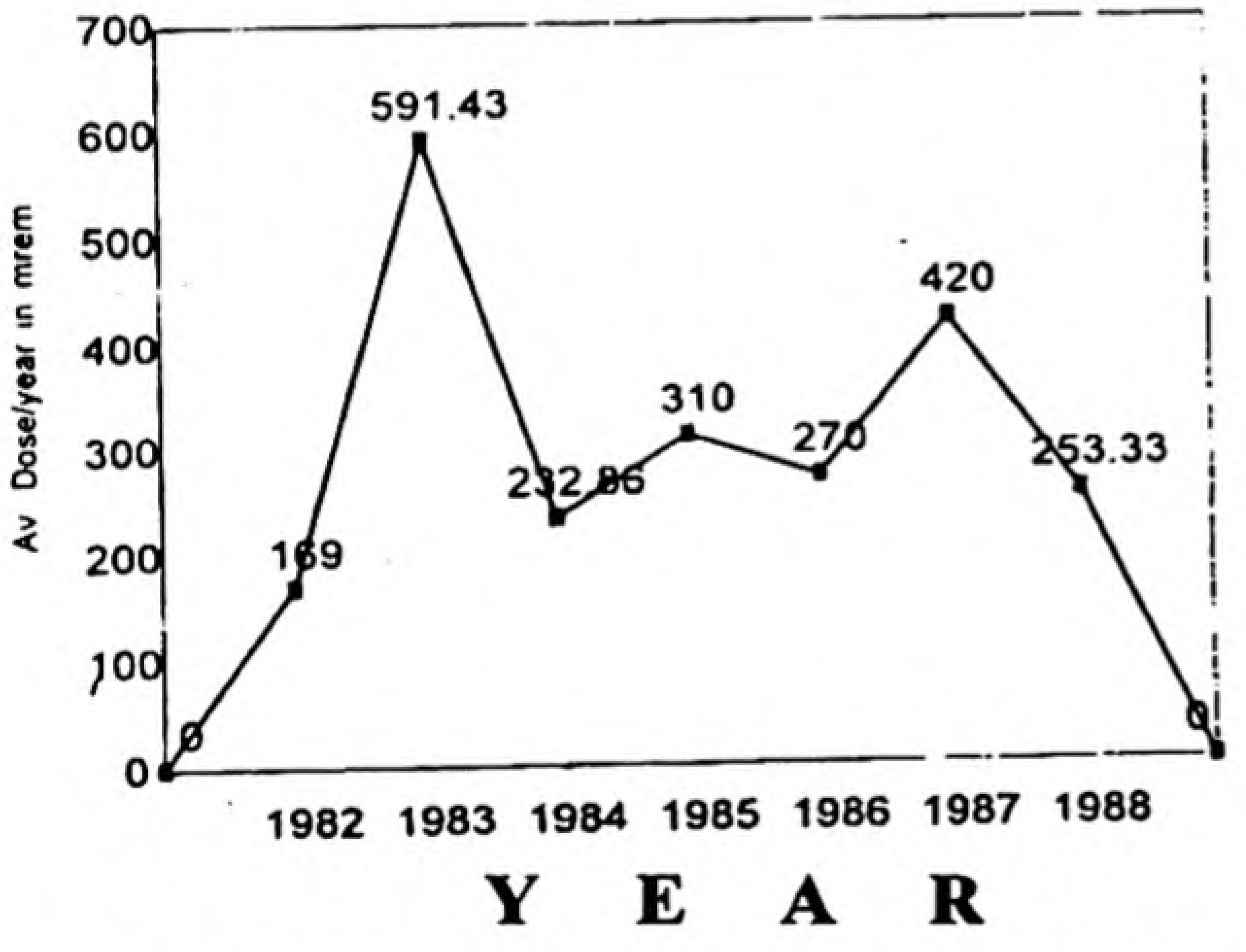


Fig.4: Personnel Working in Hot Lab. (Cagegory B)

category is involved in injecting the patients, which could give rise to higher radiation exposure. Similarly, the radiation workers belonging to category "C" of nuclear medicine department have received 57.00% more dose than the radiation workers of M.P. and B.E. department belonging to the same group. As already pointed out the former are involved in cleaning washing etc. work.

The Technologists of both the departments belonging to category "B" have received almost same dose, as all of them have same nature of work.

Lastly the radiation workers belonging to "D" group exists only in M.P. and B.E. departmen and have received only 30.83% dose to that of the maximum dose received by category "B" and are very close to category "C" of M.P. and B.E. As has been observed and discussed above, the "Technologists" belonging to "B" group of radiation workers are holding the charge of doing "Elution" of the radio-nuclides of Hot lab.and are therefore directly exposed to radiation.

Fig. 4 describes the behaviour of the average yearly radiation dose registered by the chest and wrist film badge worn by technologist belonging to category "B" It has been observed from the results that in 1982 when the department was in its initial stage (just started), work load was very less. So, the dose received by these radiation workers was only 28.57% compared to the dose received during the years 1983 (when the department was fully operational). After observing this, additional precautions were taken and good results were obtained for the following years of 1984, 1985, 1986 and the dose levels recorded during these years were of 39.37%, 52.41% and 45.10% with respect of 1983 respectively. However,in 1987 the dose level exceeded 71.01% when compared to 1983, which.was brought down to 25.95% in 1988 by adopting radiation protection safeguards and rules.

The results of the area monitoring conducted inNuclear Medicine Department at different locations using different survey meters, are shown in Table-1.

The results shown that the average dose levels in "Hot-lab." and "Waste store" is higher than the other locations (areas) in the department. Though the dose level monitored during injecting a patient is much more higher than the "Hot lab"; and "Waste Store", but the time taken to inject a patient is very little so the dose received by the "radiation workers" is proportionately less.

The dose levels were also monitored at "patient waiting". The average dose before injecting a patient was found to be only 0.75 mR/hr. While the dose level after injecting a patient (after administratintg the radioisotope injection to the patient) was found to be 3.50 mR/hr. Similarly in diagnostic examination room the average dose level was found to be 23 mR/hr near the body surface of the patient. The average dose levels monitoried at other areas in the department was found to be lying between 0.05 mR/hr to 1.5 mR/hr.

Disposal of waste

The waste of Mo-99 is disposed off in the main drain of the institute after eight half lives when the 400 mCi reduced to 1.56 mCi which goes to a water treatment plant of 7000 litre capacity. At this stage the pollution factor is 22 x 10^{-5} mCi/litre, which is well below the recommended value, though this polluted water gets further diluted when transferred to the nearby lake after treatment.

Conclusions

The present observations indicate that all the radiation workers irrespective of their category have received the dose well below the permissible limits. The average radiation dose is in accordance with their day to day nature of work and well within permissible limit. The radiation safety record and work practice is good. No accident involving radiation spillage of activity has been reported during these years. This has been due to the close co-operation between the Department of Nuclear Medicine and Medical Physics & Bioengineering Department and implementation of the radiation protection programme in the department as envisaged in the different protocol on nuclear medicine issued by International and National Authorities.

References:

1. O.P.D. Noronha. Solvent extraction technology of 99-mo 9m-Tc Generator system practical aspects of radiation protection in the hospital. Radiopharmacy during the work up of the radiopharmaceutical sodium pertechnetate 99m-Tc. Radiation Medicine Centre, B.A.R.C. Tata Memorial Centre, Annexure, Parel, Bombay AMPI Medical Physics Bulletin 1985;10: 2pp 78-85.
2. Masood Ahmad, P. Sethulakshmy & Kanta Chokra. BARC, Bombay AMPI Medical Physics Bulletin 1985;10.
3. Fred A. Mettler Jr., James H. Christie, Arvis G. Williams Jr., Robert D. Moseley Jr., Charles A. Keleey. Population characteristic and absorbed doe to the population form nuclear medicine - United States 1983. Health Physics, 1986;50:5 May 1986.
4. V. Jayalashmi, Masood Ahmad, P.N. Ramaswamy and G. Subramaniam. Current regulations in India for the procurement and use of radiopharmaceutical in Nuclear Medicine. Presented at XIII Annual Conference of Society of Nuclear Medicine. 1981; 1-3.
5. P.K. Gaur and T.V. Venkateshwaran. Measurement of Iodine-125 burden in workers from RIA laboratores. Medical Physics Bulletin 1983;8, 4.
6. F.P. Castronovo, J. R.A. Beh and N.M. Veillex. Iodine-131 therapy patient. Radiation dose to staff. Radiation Protection dosimetry 1986; 15, 1.

GHULAM RASOOL MEMORIAL LECTURE - A Tribute to Our Teachers

Farooque A Khan MB, MACP, FCCP

Introduction:

As an alumnus of the first batch of the Government Medical College, Srinagar, Kashmir, it is indeed a privilege and pleasure for me to present the first Ghulam Rasool Memorial Lecture at the meeting in Srinagar, Kashmir. While this lecture is titled Ghulam Rasool Memorial, in reality it is a tribute to all the teachers of our medical school, some of whom are no longer with us - such as 1) Dr. Ali Mohd Jan 2) Dr. Harbhajan Singh 3) Dr. Ashraf Naqshbandi 4) Dr. Hafizur Rehman, 5) Dr. Girdhari Lal, 6) Dr. Hafeezulah, and 7) Dr. Ghulam Rasool. May they all rest in peace, Ameen.

Early Memories:

Class of 70 students, mostly young boys from J&K State, few from other parts were admitted to Government Medical College in 1959. School started in Lal Mandi - current Women's Hospital. Col Gargye was advisor for GMC. Prof. Kahali in Physiology, Prof. Ayar in Anatomy.

Col. Murthi was the first principal. First two years were spent in Lal Mandi, then we moved to SMHS, and a new building was constructed to house the school. Prof. Khana: Surgery, Prof. Kaul: Medicine, Dr. Malhotra: Ob, Prof. Gujral: Pharmacology, Dr. Thaman: Peds were the department heads. First batch which was admitted in 1959 graduated in 1964; and by 1999, I guess, there are over 3,000 alumni in all parts of the world. One of the suggestions I have for GMC management is to develop a resource directory, if not done already. These alumni can be an anchor for the college.

Thanks to the efforts of Dr. G. Malik and the JK Practitioner, I have enjoyed reading the columns and keeping track of some of the alumni who have done remarkably well. To name a few who were profiled in JK Practitioner.

1. Prediman Shah - 1969 Graduate: Prominent cardiologist in the USA.
2. Ramesh Khardori - 1972 Graduate: Professor of Endocirnology, University of Illinois.
3. Arfa Rasool - 1964 Valedictorian: Prominent thoracic radiologist in New York.

Others, such as Khalida Jehangir Qazi and Muzaffar Ahmad from the 1966 batch have assumed positions of chairmanship in Medicine in Buffalo and Cleveland.

One doesn't have to look hard into reasons as to why non resident Kashmiris (NRK) do remarkably well. It's basically a response to the environment. If you plant a seed in a dry, barren land, it's not likely to grow. But if the soil is fertile with enough sunshine and water, the seed is likely to blossom into a bountiful tree. That, in essence, is the difference between the environment here in Kashmir and in the developed world. We, the NRK, will, in our own small way, attempt to change for the better the environment here, particularly in the medical area. Insha Allah.

The impact of environment first came to my notice in 1966 when my wife Arfa and I went to the USA. As newlyweds, we took a trip to Niagara Falls and walked across the bridge between the USA and Canada. In the middle of the bridge was a line showing the border between these two countries, the USA and Canada. I saw no soldiers, armored vehicles, or troops pointing guns - just civilians checking our travel documents. Having spent my entire childhood and youth in Kashmir, and having witnessed the war of 1965, it dawned on me as to what a waste of resources there was in Kashmir - army everywhere and minimal attention to basic needs of people. The rich industrialized countries, such as the USA and Canada, focused on building infrastructure and investing in people and the poor countries of India/Pakistan - destroying infrastructure and investing in armaments, even nuclear ones. Well, 33 years later nothing has improved, if anything there is deterioration.

Coming back to our medical school days, our group was always the senior most, and had the benefit of experienced teachers. I recall during our Medical clerkship Prof. Kaul, Head of the Department of Medicine, took 12 separate sessions on the 12 cranial nerves during our weekly sessions with him. His act of history taking was a classic.

There was lots of skepticism as to how the GMC

JK-Practitioner 1999; 6(4):326-329

The Lecture was delivered by Dr. Faroque A Khan Profesor of Medicine State Unviersity of New York at Stony Brook, Regent ACP. at the International Conference on Recent advances in Medicine - An Update meeting endorsed by the American College of Physicans - American Society of Internal Medicine and Medical Council of India, held at Sher-i-Kashmir Interenational Conference Centre, Srinagar Kashmir, August 21-23, 1999.

Correspondence Dr. F.A. Khan, 95 Karol Place, Jericho, New York 11753, E-mail 102100.1045@Compuserve.com.

graduate would do when they competed with graduates from more established schools. I also had my doubts; however, the results of the ECFMG exam put that to rest. Six of us from the first batch took the exam in Delhi in 1965. All six passed and got exactly the same grades on ECFMG as our final MBBS results.

Dr. Rachpal Singh, who had just returned from the states, was ecstatic when we shared this with him. A 100% pass rate from any medical school in 1965 was unheard of Remember there were no special preparation for this exam. After graduation I was assigned to Medicine. Most of us would have opted to work with Prof. Ali Jan's team (Brilliant clinician/diagnostician), but obviously all could not be accommodated on Prof. Jan's unit. My assignment was on the ward of a young dynamic physician who had just returned from the states - Dr. G.Q. Allaqaband. I recall presenting a case of a young female with congestive heart failure after delivery, "PP cardiomyopathy" to him. He gave me a good list of possibilities, but no clear dogmatic answers. This was my first exposure to American Medicine - an open mind.

It also helped that the parallel team was run by a physician trained in a different style. Most of the patients on that service were either on Antepar for worms, or steroids when Antepar didn't work. This stark contrast helped me make up my mind about my future training - the place to go was the USA.

Message here:

During your medical career, you will be exposed to teachers of all types --some are great thinkers, some great bedside teachers, some great writers. Some have lots of book knowledge, and others have excellent bedside manner.

Take values from each one, blend into your own personality, and from that will emerge good healers. As I look back at my own path in GMC, we were blessed with great teachers who cared about us. They shared with us; they took pride in our accomplishments; they more than made up for the lack of physical facilities and the rudimentary laboratory support. I am confident I speak on behalf on all of our alumni when I say, "Thank you." Prof. Brij Mohan Bhan actually spent five years teaching us first in Anatomy, and then when we moved to SMHS for clinical he also moved and joined the surgical department. A special thanks to Prof. Bhan.

Now let met spend the remaining time on one teacher, Dr. Ghulam Rasool, whose life and accomplishments wrap together both the struggle of Kashmiris and their accomplishments.

Dr. Ghulam Rasool was born in Srinagar. His father was Mian Mohd. Iqbal. Ghulam Rasool passed B.Sc from S.P. College and then completed his MBBS at KE Lahore Punjab University, 1933-1938. Married to Ruqaya September 15, 1939. He was sent on deputation to the UK oy Chief Minister Sheikh Abdullah and obtained FRCS in 1957.

After graduation from KE Medical College, Dr. Ghulam Rasool was unable to get a job in government service in J&K State. He joined a missionary hospital, which is current Drugan Chest Hospital, and worked with Dr. Waras who stimulated his interest in surgery. An unexpected opening in J&K Service led to his joining the J&K Service, but his did not last. He lost this job and once again went back to Missionary Hospital. Finally for the second time, he joined J&K Service once again and worked at SMHS Hospital, which I am told at that time was in a different location in Lal Mandi.

He was then transferred to Skardu and, after an arduous journey on horseback, Dr. Ghulam Rasool, his young wife and three children reached Skardu where he worked long hours, obtained great surgical skills and speed, and with limited support and staff he had to improvise. Example: Performed C-section on a patient with a house knife, scissors and silk thread. The woman survived and used to visit him for many years after that.

After one year in Skardu, Dr. Ghulam Rasool was transferred to Gilgit and his family wanted to visit relatives in Srinagar before leaving for Gilgit - that was August 1947. The conflict over Kashmir resulted in the establishment of a line of control, the division of J&K State, and Dr. Ghulam Rasool's live, life so many others at that time and afterwards, was changed forever. Had they not come for a family reunion to Srinagar, they would have been in Gilgit and employees in Gilgit at that time became part of Pakistan Civil Service.

In the early 50's, Dr. Ghulam Rasool was sent on deputation by the J&K government to the UK where the obtained his FRCS. He was the first one from Kashmir to do so in the surgical field. After his return, Dr. Ghulam Rasool and his contemporary, Dr. Girdhari Lal, became the two leading surgeons in Kashmir, competitors who respected each other greatly and ruled the surgical wards 15-20 in SMHS.

As a surgeon Dr. Ghulam Rasool was up-to-date, innovative and a fast operator. He was the first one to report "Kangri cancer" - unique to only Kashmiris. His gastrectomy procedure was a treat to watch, as was his surgery on thyroid. His assistants always remembered his deep, penetrating and fixed glare of his bright eyes that showed through his thick glasses. His special interest in thyroid had earned him the nickname "Hashimorto". I remember, as a surgical clerk, watching in awe as he removed a huge hydatid cyst of the liver in a young woman from Ladekh under local anesthesia. Because of his speed, he was able to perform -12-15 surgeries a day. He was blessed with a healing hand and his patients made miraculous recovery.

The two surgical leaders soon had to face the reality of having to deal with the challenges posed by beginning of the new "GMC". There were new bosses to deal with - Prof. Khanna was the new chair of Surgery, Dr. Ghulam Rasool was Associate Professor. It must have been hard on them. However, Dr. Ghulam Rasool rose to the challenge and eventually became the HOD of the Surgical Department. His tenure at SMHS was marked by the cadre of young staff who took a deep interest in the field of surgery, and many of them have now developed into leaders in their own fields.

Dr. Ghulam Rasool was a man of simple habits. He, for many, years, used to ride to SMHS on his bicycle; and, on occasion as a medical student, I drove past him. Eventually a family car was purchased and it was always a sight to see - Dr. & Mrs. Ghulam Rasool and their six children ride in the car, a "Fiat". Dr. Ghulam Rasool's driving skills, however, were not at par with his surgical skills. Dr. Ghulam Rasool was very, involved in his professional work. Managing or being involved in the affairs of the house were not in his personality. His wife did that job superbly. Then there was the issue of his temper. He had, as we would say in the states, a short fuse; and smart employees learned to keep their distance during these outbursts. As an administrator, he was hard working honest, and a strict disciplinarian who took a keen interest in every aspect of hospital affairs. During his tenure the SMHS was spic and span, visiting hours were respected (once he turned out his own son who was visiting his friend in the hospital off hours), and food was of high quality (once he beat up the milk man who had added water to milk).

He was not very astute politically and did not curry favours with his "bosses", for which on several occasions he paid a heavy price. His children performed exceptionally well in academics, and when they got involved in the political life as students, Dr. Ghulam Rasool had to pay the price. He was twice transferred to Jammu because of the political activism of his son, Aijaz, and daughter, Abida.

Dr. Ghulam Rasool was responsible for the idea of having a separate bone and joint hospital, pediatric and women's hospitals, and was involved in the initial planning of the Soura Institute, as well.

After over 30 years of distinguished service, Dr. Ghulam Rasool retired on August 19, 1973, and he lived a retired life for over two decades. This time was spent mostly with his children who, by then, had settled in several parts of the world-Zahida, a pediatrician, in New York; Arfa, a Radiologist, in New York; Abida, a physicist by training and a business woman by vocation, in Saudi Arabia; Rabia, a pathologist, in New York Aijaz an engineer, here in Kashmir; and Ayaz, a urologist, in New York, who inherited his Dad's surgical skills. Dr. Ghulam Rasool was married 55 years to Ruqaya Rasool.

In summary, Dr. Ghulam Rasool led a productive, meaningful life. He made major contributions to the medical profession here. He left behind a legacy and ocean of good will. Most importantly, he left behind a devoted family who continues in the traditions he left behind. In the Islamic tradition it is mentioned that a person who leaves behind.

1. a pious child who prays for the deceased parents,
2. an institution of learning,

has "made" it. Dr. Ghulam Rasool certainly did that, and in consultation with some members of his family - most significantly his second daughter, Arfa - I, as one of his students, would like to propose the following for your consideration.

1. **Annual Lectureship:**
   The Arfa and Faroque Khan Foundation in New York will establish an annual lectureship in Dr. Ghulam Rasool's honor. The format and details will, Inshah Allah, be developed in consultation with key medical leadership here in Srinagar.

2. **Student Awards:**
   An annual award will be given to a medical student of any medical school in Kashmir who prepares an award-winning essay, accepted for publication in JK-Practitioner, and focuses on some aspects of medical care in J&K State. The details will be published in a future issue of JK-Practitioner.

3. **Illm Convention**
   Hyderabad, mid-January 2000-Support one attendee's travel, lodging, registration. This awardee will be expected to prepare a succinct summary of the conference for publication in JK-Practitioner. Dr. Ghulam Rasool had a keen interest in Islamic history and values.

Besides these three specific proposals, I would like to summarize for you some of the other ideas and proposals that the NRK - non-resident Kashmiri doctors - and the senior physicians here have been discussing, and we will share this with the rest of the NRK's in the USA.

1. **Establishment of Mini-fellowships**

   As a Regent of ACP, I have been encouraging ACP - ASIM to help establish the concept of mini-fellowships. I have travelled to the Middle-East and South America as a representative of ACP and, invariably, I get asked the same thing - could you help us get our bright young physicians for short-term training to the USAP I can assure you that this is receiving serious consideration, and a proposal by Dr. Rudolfo Armas, ACP Governor from Chile, is under review, and when it gets adopted by ACP-ASIM I can assure you that this part of the world will receive priority. I envision the following mechanism -Let's assume one of you wants to get three months, special training in spiral CT/BMT/ MRI. Well, you would write to ACP: they would have a list of institutions willing to host you; they - ACP - would connect you with them. Once accepted, ACP would facilitate visa, etc., and you would come for the mini-fellowship. The ACP will NOT funds this. That's where we, the NRK, come in the picture. The NRK would help pay support for your board, lodging, perhaps some transportation. This concept, I believe, is workable, and I believe mutually beneficial. Thanks to the efforts of Abdul Rauf Mir, a young surgeon Tajamul Fazli spent several months in the USA learning new techniques for renal transplants. These efforts have already paid rich dividends with recent successful renal transplants.

2. **Equipment Supplies Etc.**

   We have and will continue to send you available portable medical equipment. Drs. Bukhari, Mushtaq Shah, G. Jeelani Dhar, and others have done so, and we will certainly expand the scope of it.

3. **Educational Material**

   We have sent some journals, books, etc. However, now with the introduction and spread of electronic communication I feel we should work towards helping you establish proper set up in your libraries so that you can access to the various medical information pieces which are proliferating in abundance. We could, for a future meeting, consider having a symposium on Medical Informatics. I know my colleague, Regent Ted Shortliffe, who runs the Medical Informatics at Stanford University would be happy to visit and share his knowledge with you.

4. **Curriculum Support**

   Many of us teach at medical schools in the USA. For example, I have been involved with student education at Stony Brook since 1971. With some organization restructuring of your curriculum, there is no reason why others and I would not be able to share our expertise regarding various diseases with students here-not for one session, but over several weeks time.

5. **Non-academic, Non-procedure NRK**

   If we had a proper set-up here with appropriate diagnostic facilities, we could have the visiting NRK see referred patients on a consultation basis.

6. **ACP-ASIM International Forum**

   Dr. Watler McDonald's Executive Vice-President of ACP-ASIM, message outlines some new ACP-ASIM international initiative. I invite you to submit an abstract. If accepted for presentation for an ACP national meeting, we will help you with logistics.

7. **Mental Health Workers**

   The Bosnia experience has taught us the importance of attending to post-traumatic stress disorder that, in my view, is rampant here. We are willing to sponsor and train mental health workers for this important task.

These are just some ideas that we would like to leave with you, and with the dilligence and perservance of physicians like Dr. G.M. Malik and Dr. M.A. Kamli, who were instrumental in making this conference possible, I am confident at future meetings we will not just be presenting ideas but looking at outcomes of our efforts. I often like to use the analogy of the three kinds of people.

1. Watch things happen.
2. Wonder what happened.
3. Make things happen - Let us all stive towards making this happen.

In closing, I must admit most of the NRK's who participated in this conference had some misgivings, particularly after the Kargil episode. I am very happy we came. I have seen a catharsis for the professionals working under tough conditions. I have witnessed a healthy professional exchange and interaction. With your continued enthusiasm, I am confident many of us will return for longer periods of time. Insha Allah

POST GRADUATE TRAINING FOR OVERSEAS DOCTORS IN THE UNITED KINGDOOM

Mohd Afzal Mir M.B.B.S., DCH, FRCP.

The quest for knowledge has always taken man to the different parts of the world away from his homeland. The Medical Science is an ever changing field and doctors, since times immemorial, have travelled thousands of miles in order to keep pace with the recent developments. The United Kingdom has been a popular destination for doctors from all over the world to get higher training in the different specialities. Postgraduate training in the United Kingdom is considered to be amongst the best in the world, and returning home with a specialist degree or diploma enhances the chances of success in the employment or independent practice.

Reason for entry to the United Kingdom can be summarised as follows:

1. To acquire general and specialist traning in a medical/ surgical/other specialities.
2. To obtain higher examinations such as Member of the Royal College of Physicians (MRCP), Fellow of the Royal College of Surgeons (FRCS), etc.
3. To acquire Certificate of specialist training such as Certificate of Completion of Specialist Training (CCST).
4. To learn advanced skills and technology.
5. To undertake a period of research.

The General Medical Council (GMC).

The General Medical Council is the body which keeps and publishes a register of qualified doctors, It also establishes the standard of education and experience required for inclusion in the register and promotes high standards of medical education. Evidence of registration with the GMC is mandatorybefore undertakingdirect patient care in the UK. There are 3 forms of registration with the GMC.

1. Provisional Registration

All graduates of the UK who are doing pre-registration (=intern) house officer job are given provisional registration that is changed direct to full registration after completion of one year of house officer jobs in Medicine and Surgery.

2. Limited Registration

The majority of overseas doctors coming to the UK for training will have a qualification which is accepted for the purpose of limited registration only. The limited registration is for a maximum period of five years and can be achieved by pursuing one of the following approaches:

a. Pass the Professional and Linguistic Assesement Board (PLAB) Examination.
b. Get exemption from the PLAB Examination.
c. Hold a higher qualification offered by one of the Royal Colleges or faculties in the UK or Republic of Ireland which is registrable with the GMC i.e. MRCP, MRCS etc.
d. Doctors who have been qualified and have practiced overseas for at least 10 years and reached a Consultant grade or equivalent can apply for Limited Registration.

3. Full Registration.

All Graduates of the UK are given full registration after having completed 1 year as a pre-registration house officer. Doctors with limited registration can progress to full registration after satisfying the GMC.

PLAB Examination

The PLAB test is conducted by the Professional and Linguistic Assessment Board. The standard required to pass the test is defined by the board in the following terms:

A Candidate's command of the English language and professional knowledge and skill must be shown to be sufficient for him or her, to undertake safely employment at first year Senior House Officer level in a British hospital.

Admission to the PLAB is open to doctors whose

JK-Practitioner 1999;6(4):330-332
From the University Hospital of Wales Cardift (UK) (Mir)
Recieved June 1999 Accepted August 1999

primary medical qualification is accepted by the GMC for the purpose of limited registration. These primary medical qualifications listed in the world directory of medical schools, which is published by the World Health Organisation.

Before entering the test, a doctor will be normally expected to have completed, in countries outside the UK, a minumum of 12 months postgraduation clinical experience.

Description of PLAB examination

The overall layout of the PLAB test is:

1. *English launguage Test.* It is conducted by the International Language Testing System (IELTS). It has 4 components i.e. writing, reading, listening and speaking.The GMC will require a minimum overall band score of 7.0, with a minumum score of 6.0 in each of the 4 individual sections.

2. *Medical Component:* It consists of two parts.

Part 1

There are 3 medical written papers in Part 1.

a. Multiple Choice Questions.
b. Clinical Problem Solving.
c. Photographic material examination.

To pass part 1 all 3 papers must be passed at a single sitting.

IELTSS and the Part 1 of PLAB test can be taken in different centres all over the world including the ones in India.

Part 2

Doctors who pass IELTS and the part 1 of PLAB test are eligible to apply for entry to part 2, an objective structured clinical exmamination (OSCE), which is taken only in the UK. The aim of the PLAB OSCE is to test the candidate's clinical and communication skills in a number of controlled situations. Candidate is required to rotate around a circuit of 12 stations. Each station represents a particular clinical situation and may involve a patient or anatomical model.

PLAB test exemption

The GMC gives exemption from the PLAB test to doctors of exceptional ability, provided they are sponsored by one of the Medical Royal Colleges. Other acceptable sponsoring bodies are the British Council, the Commonwealth Scholarship Commission, the Department of Health, on behalf of the World Health Organisation and Council of Europe and certain universities in respect of research appointments. A consultant wishing to sponsor a doctor must get in touch with one of the acceptable sponsoring bodies. Doctors who have previously failed the PLAB test are not normally considered by the GMC to be suitable candidates for sponsored exemption from the test.

Basic Specialist or general professional training

This is the grade most commonly filled by overseas doctors arriving in the UK. Basic Specialist or General Professional training is delivered through the Senior house officer or equivalent grade. Uusally posts are of 2 or 3 years duration, often rotational posts but some jobs are free standing for 6 months at a time. During this period the trainee is expected to complete the postgraudate degree/diploma of the Royal Colelges or Faculties.

The aims of the SHO Training are:

- To get wide clincial experience and a number of generic skills under supervision.
- To develop communication, presentation and leadership skills.
- To develop interest in and knowledge of research and the importance of evidence based practice.

An overseas doctor engaging in basic specialist or general professional training is granted initial permit free training visa not exceeding 3 years. However there is an aggregate maximum limit of 4 years permit free training in this grade.

Higher Specialist training.

Higher Specialist training follows basic specialist or General Professional Training and is delivered through the Specialist Registrar or equivalent grades.

All Overseas doctors within the specialist registrar grade are referred to as Visiting Specialist Registrars (VSpR). There are 2 types of programmes to which overseas doctors may be appointed, both require that a doctor meets minimum entry criterion.

Type 1 Training

This is a specialist training programme which if completed satisfactorily may entitle the doctor to the award of the Certificate of Completion of Specialist Training (CCST). Trainees in this programme are subject to annual assessment. At the end of each year an interview is held and the decision is made as to whether the trainee has made satisfactory progress and can proceed to the next year of training, or whether he or she needs specially focused training for which they may be held back. An overseas doctor in this programme is given an initial grant of 3 years of permit free training visa and further extension if necessary to complete the requirements for the CCST.

Type 2 training

This is also called Fixed Term Training Appointment (FTTA) and is only available to those without the right of permanent residence in the UK. The aim of this programme is to allow the trainee to pursue a modified training programme tailored, where practicable, to meet the individual doctors training goals. Individuals appointed to an FTTA will receive Permit free training visa for the length of the FTTA which can vary from 6 to 24 months or longer to fulfill individual needs.

The Certificate of Completion of Specialist Training (CCST)

Once doctors have completed a defined training programme successfully they can then apply to the Specialist tranining Authority for award of a CCST in the relevant speciality. This only applies to those who have completed a type 1 programme. For the UK doctors and overseas doctors with the right of indefinite residence in the UK, the General Medical Council places name of the person with the CCST on the Specialist Register and they are then eligible to apply for a consultant post.

The overseas doctors without the right of indefinite residence in the UK, are awarded the CCST but do not have their name placed on the specialist register. The are expected to leave the UK.

Dr. Manzoor S Qazi, President Jeddah Orthopedic Club has in a letter to the Principal, Govt. Medical College, Srinagar with a copy to the Editor JK-Practitioner, confirmed the sponsoring of two orthopedic surgeons for fellowship in orthopedics (Arthoscopic surgery) of 4-6 week duration. He has also indicated to donate the arthoscopic equipment to the Bone and Joint Hospital, Srinagar after the doctors are trained. The expenses will include return air fare (Delhi-Jeddah) besides providing for food and accommodation. For details apply to Principal, Govt. Medical College, Srinagar/Chief Editor JK-Practitioner, Batmaloo, Srinagar.

UPDATE IN ALLERGY AND IMMUNOLOGY

Mark T. O'Hollaren, M.D.

We are just beginning to understand the associations between the immune system's physiology and clinical symptoms. This knowledge is facilitating the development of new therapies for allergic disorders. We begin with a review of new guidelines for the asthma therapy that, in part, stem from our new understanding of immune pathophysiology. We then review several advances in asthma therapy related to medication timing, longer-acting inhaled β_2 agonists, and leukotriene antagonists and summarize current thinking on mortality related to asthma. We discuss the immune response in allergic rhinitis, the role of inhalant allergens in allergic rhintis. Finally, we address latex allergy, a growing clinical problem for health care works.

Asthma

Asthma affects up to 15 million Americans and is the most common chronic disease of childhood. It accounts for more than 100 million days of missed school or work, results in 470 000 hospitalizations a year, and causes more than 500 deaths annually.

Second National Heart, Lung, and Blood Institute Guidelines Were Issued

Guidelines for the Diagnosis and Management of Asthma: Expert Panel Report 2. Bethesda, MD: U.S. Department of Health and Human Services. Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; 1997. NIH publication no. 97-4051.

The National Heart, Lung, and Blood Institute's National Asthma Education and Prevention Program convened two expert panels to prepare guidelines that provide physicians and other health care professionals with recommendations, based on scientific evidence, to aid in the diagnosis and management of asthma. Their reports were issued in 1991 and 1997. A summary of the 1997 recommendations follows

It is now known that asthma is a chronic inflammatory disorder of the airways whose symptoms and signs result from a complex interaction of many cells and their components. These include mast cells, eosinophils, T lymphocytes, neutrophils, and epithelial cells. This inflammation causes an increase in bronchial hyperresponsiveness to a variety of specific and nonspecific stimuli. The diagnosis may be established when at least partially reversible episodic symptoms of airflow obstruction are present and alternative diagnoses are excluded (Table I).

In the 1991 guidelines , asthma was classified as mild, moderate, and severe; in the 1997 guidelines, the classifications were changed to mild intermittent, mild persistent, moderate persistent, and severe persistent. The panel stressed that patients at any level of disease severity may experience a severe exacerbation

The 1997 report emphasizes the importance of using objective measures of disease severity and the fact that physicians who care for patients with asthma need to follow patient progress with spirometry for the purpose of diagnosis and office monitoring, In selected patients, peak expiratory flow rates may be monitored to determine diurnal variation as well as variation over time. Decreases in peak expiratory flow rates to less than 80% of a patient's personal best rate generally indicate a need for additional medication, and decreases to less than 50% of a patient's personal best rate indicate a severe exacerbation.

The panel recommends that, at a minimum allergens that may contribute to asthma be identified in patients requiring daily medication, with appropriate avoidance advice and, in selected cases, allergen immunotherapy. Avoidance of allergens identified by skin testing is important in the overall treatment plan of patients with allergen-induced asthma. Although valuable, the clinical history alone is not a reliable method of determining all relevant allergen triggers (Table 2).

Panel recommendations for pharmacotherapy include a stepwise program beginning with as-need use of β_2 agonists for mild intermittent asthma and progressing to a multifaceted program for severe persistent asthma.

JK-Practitioner 1999; 6(4):333-337
Repreoduced with the Permission of Pamelx W Fried, Director, Journal Publishing
ACP-ASIM From Ann. Intern Med 1988;29:1036-1043.

Table 1. Differential Diagnostic Possibilities of Asthma in Adults*

Chronic obstructive pulmonary disease (chronic bronchitis or emphysema)
Congestive heart failure
Pulmonary embolism
Laryngeal dysfunction
Mechanical obstruction of the airways (tumors)
Pulmonary infiltration with eosinophilia
Cuugh secondary to drugs (angiotensin-converting enzyme inhibitors)
Vocal Cord dysfunction

Data obtained from Guidelines for the Diagnosis and Management of Asthma. Expert Panel Report 2.Bethesda MD. US. Department of Healthand HumanServices, Public Health Service, National Institutes of Health, NationalHeart. Lung, and blood Institute. 1997. NIH publication no. 97-4051.

Daily Late Afternoon Steroid Dosing is as Effective as Four-Times-Daily Dosing

Pincus DJ, Humeston TR, Martin RJ. Further studies onthe chemotherapy of asthma with inhaled steroids: the effect of dosage timing on drug efficacy. J Allergy Clin Immunol. 1997;100(6 Pt 1):771-4.

Adrenal glucocorticoid production is greatest near dawn, and several studies have shown varying effects of inhaled and oral glucocorticoids when the drugs were used at various times during the day. In this three-part study, Pincus and colleagues gave 800 ug of inhaled triamnicinolone to 60 patients with documented asthma. The three regimens were 200 ug four times daily, 800 ug given at 8 a.m. and 800 ug given at 5:30 p.m. The results showed that morning peak expiratory flow rate improved 14% in the four-times-daily group, improved 4% inthe 5:30 p.m. group, and did not change in the 8 a.m. group. Evening peak expiratory flow rate improved 4% in the four-times-daily group, 5% in the 5:30 p.m. group, and 2% in the 8 a.m. group. Although morning improvements in peak expiratory flow rates were smaller with once-daily than with four-times-daily dosing, the former regimen could be considered in patients for whom compliance is a problem.

Long-Acting β_2 Agonists Were Superior to Short-Acting B_2 Agonists in Milder Asthma

Boulet LP, Laviolette M, Boucher S, et al. A twelve-week comparison of salmeterol and salbutamol in the treatment of mild-to-moderate asthma: a Canadian multicenter study. J Allergy Clin Immunol. 1997;99:12-21.

The National Heart, Lung, and Blood Institute guidelines emphasize the use of long acting inhaled B_2 agonists for moderate to severe persistent asthlma. Less emphasis is placed on such treatment for milder asthma, but Boulet and colleagues sought to determine the effects of long-acting β_2 agonists in patients with this type of asthma.

In a multicenter clinical trial, 228 patients with mild to moderate asthma (mean FEV_1, 66% of predicted) were randomly assigned to receive either salbutamol, 200 ug four times daily, or salmeterol, 50 ug twice daily, for3 months. Salbutomal is similar to albuterol and has clinical activity for 4 to 6 hours; the activity of salmeterol averaged about 12 hours. Patients were assessed at 3 to 6 hours and 10 to 12 hours after treatment to ensure that dose effects were minimized.

Table 2: Sample Questions for the Diagnosis and Initial Assessment of Asthma*

In the past 12 months,
- Have you had a sudden severe episode or recurrent episode of coughing. wheezing (high-pitched whisting sounds when breathing out), or shortness of breath?
- Have you had colds that "go to thechest" or take more than 10 days to get over?
- Have you had coughing, wheezing, or shortness of breath during a particular season or time of year?
- Have you had coughing, wheezing, or shortness of breath in certain places or when exposed to certain things (e.g. animals, tobacco smoke, perfumes)
- Have you used any medications to help you breathe better? How often? Are you symptoms-relieved when the medications are used?

In the past 4 weeks, have you had coughing, wheezing, or shortness of breath
- At night that has awakened you?
- In the early morning?
- After running, moderate exercise, or other physical activity/

** A 'yes" answe rto any question suggersts that any asthma diagnosis is likely. These questionls are examples; their validity has not been formally assessed. Data obtained from: Guidelines for the Diagnosis and Management of Asthma. Expert Panel Report 2. Bethesda, MD: U.S. Department of Health ad Human Services, Public Health Sercice, National Institutes of Health, National Heart, Lung, and blood Institute. 1997. NIH publication no. 97-4051.*

The FEV_1 improved more substantially in the salmeterol group. The initial effect of salbutamol was equal to that of salmeterol, but FEV_1 dwindled steadily too near-baseline values by the time a second dose was required. Patients taking the longer-acting drug experienced no volleys in effect. Morning peak expiratory flow rate, days without symptoms, and absence of night time awakening were all superior among those taking salmeterol.

Thus, it seems that a second-line drug for patients with mild to moderate disease should probably be a long-acting β_2 agonist such as salmeterol, usually used with an inhaled anti-inflammatory agent. First-line treatment remains anti-inflammatory therapy if short-acting bronchodilators are needed more than two to three times per week (Table 4).

Role of Leukotriene Antagonists is Still Being Clarified

O'Byrne PM, Israel E, Drazen JM. Antileukotrienes in the treatment of asthma. Ann Intern Med. 1997;127:427-80.

A major pathway of inflammation is the arachidonic acid cascade, which has a cyclooxygenase pathway and a leukotriene pathway. The later results in at least four leukotrienes, at least three of which have been associated with asthma. Several leukotrience antagonists are now clinically available, but their ideal place in asthma treatment remains unclear.

In a systematic review of the evidence indicating that leukotriene antagonists are safe and efficatious in patients with asthma, O'Byrne and colleagues synthesized data from clinical trials reported through 1996. Published data revealed sound evidence that leukotriene antagonists were clinically active in patients with exercise-induced, and aspirin-induced bronchoconstriction and that these effects were additive to those caused by β_2 agonists. Leukotriene antagonists have occasionally been associated with elevated hepatic enzyme levels, although hepatic failure is extremely rare. Case reports have also suggested a rare association between leukotriene anatagonists and eosinophilic pneumonia.

The data reviewed are helpful, but further work is needed to establish the ideal role of leukotriene anatagonists in asthma treatment. These agents seem particularly helpful, in patients with "triad asthma" (asthma, nasal polyps, and aspirin sensitivity). Their role in managing severe asthma may increase as more data become available.

Asthma Mortality was Usually a Result of Inappropriate Treatment

McFadden ER Jr, Warren EL. Observations on asthma mortality. Ann Intern Med. 1997;127:142-7.

Despite the increasingly aggressive treatment of asthma, rates of death from asthma have increased (although the mortality rate in the United States is lower than that in most developed countries). In this paper, McFadden and Warren reviewed what is known about asthma mortality.

During the past 30 year, U.S. and Canadian case-fatality rates have remained a little less than 2 deaths per 100.00 patients. In the past decade, however, the U.S. case-fatality rate has increased from 1.3 to 1.9 per 100.000, a 46% increase but still a small number of deaths compared with the mortality rate of many other pumonary diseases (for example, lung cancer kills more than 30 times as many persons annually). Of note, whereas most asthma deaths occur in patients with known severe disease, deaths occur even among those with asthma that had been consdered very mild.

Mortality rates vary markedly among regions and ethnic groups. New York and Cook County, Illinois accounted for 21% of all asthma deaths in the United States. Other cities with high populations of poor and minority citizens had disproportionately high number of deaths. The highest death rates are in African-American men.

Most patients die in the hospital, and evidence shows that the greatest threat to life is inappropriate or delayed treatment. Little evidence supports other potential causes of death, including medication side effects, tachyphylaxis to inhalers, and β_2 associated cardiac arrhythmias. Harbingers spending disaster are a pretreatment arterial saturation of less than 90% normal or PCO2 levels after treatment, persistent metabolic acidosis, and severe obstruction that does not improve by at least 30% to 40% after treatment with sympathomimetic agents.

The prognosis after a near-fatal asthma episode and restart nasal steroid therapy at about half the previous dose. If epistaxis recurs, alternative therapy should be used.

Systemic steriod treatment, especially depot injections, was once given at the onset of a patient's allergy season. Depot injection is cost-effective, and patients may like the convenience. However, it has many problems. First, it has been associated with subcutaneous atrophy and, with prolonged use, osteoporosis. Second, absorption of depot preparations is not completely predictable. Third, the advent of effective topical steroid therapy has decreased the necessity of using systemic steroid therapy for allergic rhinitis.

Nasal ipartropium bromide helps relieve rhinorrhea but is generally not effective for other nasal symptoms, such as congestion and sneezing. Allergen immunotherapy may be used when symptoms are prolonged during the year, are excessively severe or incapacitating, or are not adequately controlled by pharmacotherapy. The effectiveness of allergen immunotherapy in allergic rhinitis, directed against dust mites, molds, pollens, and animal danders, has been clearly documented. Potential systemic reactions are highly unlikely with careful dose titration and monitoring in the hands of physicians familiar with its use.

Recent data also suggest that indoor allergen levels are important in the sensitization to common allergens, such as cat dander and dust mites. Furthermore, in persons with an allergic disposition (for example, those with a strong family history of allergic disease), allergen avoidance early in life may prevent sensitization. Allergen immunotherapy has also been shown to alter the natural course of allergy in children by helping to prevent the development of new sensitizations to other allergens[2]. Altering the natural course of allergic disease and asthma is an exciting new area of research. As our understanding of the impact of immunotherapy on various aspects of the allergic inflammatory process becomes clearer (for example, effects on adhesion molecule expression and eosihophil recruitment), we should expect to move closer to that goal.

Rhinitis Was Linked to Asthma

Corren J. Allergic rhinitis and asthma: how important is the link? J Allergy Clin Immunol. 1997;99;5781-6.

Many practicing allergists and primary care physicians recognize that patients often have both allergic rhinitis and asthma. Corren synthesized the current knowledge of this association and the implications for treatment and research.

Epidemiologic studies show that up to 78%of patients with asthma also have rhinitis symptoms and up to 38% of patients with allergic rhinitis have asthma symptoms. The studies have also shown a temporal relation between the two conditions. Rhinitis tends to predate asthma in most patients. Rhinitis ends to predate asthma in most patients, and ongoing exposure to an allergen may increase the risk for subsequently developing ashtma. The observation that treatment of allergic rhinitis may also alleviate asthma symptoms has increased interest in the asociations between these two respiratory disorders. The administration of intranasal steroids during the pollen season can prevent the increrases in nonspecific bronchial hyperresponsiveness normally seen during that season. In patients with perennial rhinits, intranasal steroid therapy reduces daily asthma symptoms, exercise-induced bronchospasm, and bronchial responsiveness to methacholine. The mechanisms underlying these observations are not clear.

Nasal allergen provocation may also increase lower-airway reactivity within 30 minutes, suggesting a possible neural reflex. Improvements in lower-airway fuction after treatment of upper-airway symptoms may result from improved warmingand humidification of inspired air, decreased inhalation of inspired allergens, a decreased nasal-bronchial reflex, or other mechanisms. Postnasal drainage of inflammatory cells during sleep may also affect the responsiveness of the lower airways. Future research is needed to determine the extent to which treatment of upper-airway allergy alters the natural history of asthma.

Other conditions have strong associations with allergic rhinitis[3]. These include chronic sinusitis and otitis media, both of which respond to treatment of the rhinitis: upper respiratory tract infections: and nasal polyposis.

Latex Sensitivity

Immediate IgE-mediated allergic reactions to latex products have become increasingly recognized in medical workers and others who have begun to use rubber latex gloves more routinely. Latex gloves are the largest single source of exposure to these allergens, which may trigger reactions ranging from symptoms of mild allergic rhinitis to severe anaphylaxis resulting in death. In most case, sensitization to latex proteins is related to exposure to latex-glove allergens. Exposure may occur through direct contact with an offending device or through inhalation of the latex allergen, which may be "carried" by the corn starch powder used in most powerdered latex gloves. Ongoing exposure to latex proteins may also result in occupational asthma to the proteins. if exposure continues, asthma may progress to the point of persistent impairment or disability.

More than 5% hospital workers develop clinical allergies to latex and continue to remain in contact with latex proteins[4]. Dental students and faculty are also at high risk for latex sensitization[5]. An increasing duration of exposure correlates with an increasing risk for sensitization and development of latex allergy.

In the 1997, the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology issued a joint statement regarding this increasingly common problem. The guidelines propose that latex gloves should be used only as mandated by accepted universal precuations. The routine use of latex gloves by personnel in low-risk situations (food preparation, housekeeping, patient transport, and routine physical examination) should be discouraged.

When these gloves are necessary, the statement proposes that only low-allergen, powder-free latex gloves be worn.This practice will reduce the reaction rate among persons who are already sensitized and mayreduce the rate of sensitization. Using powder-free latex gloves will decrease the airborne levels of latex allergen and should also decrease the risk for both sensitization and reactions in those already sensitized.

Summary

Internal medicine has witnessed astounding developments in our understanding of the immune system's role inthe pathophysiology of many diseases. The present challenge is to harness this knowledge to develop more effective therapies for immune-related illness. Guidelines for the care of common illnesses such as asthma may encourage appropriate clinical application of advances in our armamentarium against immune disease.

Requests for Reprints: Mfark T. O'Hollaren, MD, Department of Medicine. Oregen Health SciencesUniversity, OP30, 3181 SW Sam Jackson Park, Portland, OR 97201.

Current Author Addresses:Dr,O'Hollaren:Allergy Clinic, 511 SW 10th Avenue, Suite 1301, Portland, OR 97205.

Dr. Roberts (Series Editor): madrona Medical Group, 3199 Steller Court, Bellingham, WA 98226.

References:

1. Hill DJ, Thompson PJ, Stewart GA, Carlin JB, Nolan TM, Kemp AS, et al.The melbourne house dust mite study: eliminating house dust miles in the domestic environment J. Allergy Clin Immenol 1997;99:323-9.
2. Des Raoches A,Paradis L, Menardo JL. Bouges S, Daures JP,Bousquent J. Immunotherpy with a standarized Dematophaoids pteronysinus extract: VI Spectic immunotherpy prevents the onset of new sensitization in children J Allergy Clin Immunol. 1997;99: 450-3.
3. Spector S. Overview of comobid asociateionsofallergic thinits. J Allergy Clin Immunol 1997;99:5223-80.
4. Kibby T, Ak, M. Prevalenceof latex sensitization ina hospital employee populationAnn Allergy Asthma immunool 1997;78:41-4.
5. Tarle SM, SussmanGL, Holness DL. Latexsensitivity in dental students andstaff crisssectional study J. Allergy Clin Immun 1997;99:396-401.

Abstracts:

ROLE OF INFLAMMATION AND METALLOPROTEINASES IN PLAQUE DISRUPTION AND THROMBOSIS

Vascular Medicine 1998;3:199-206

Prediman K. Shah

Nymerous pathologival, clinical, angiographic and angioscopic studies have demonstrated that acute coronary syndromes (unstable angina, acute myocardial infarction a ischemic sudden death) are most frequently the consequence of plaque disruption (plaque rupture or superficial plaque erosion) and consequent coronary thrombosis. Several serial angiographic studies have demonstrated that nearly 60-70% of acute coronary syndromes evolve from mildly to moderately obstructive atherosclerotic plaques (plaque disruption appears to be a function of bothe the composition of the plaque (plaque vulnerability) as well as ectrinsic triggers that may precipitate plaque disruption in vulnerable plaque. Vulnerability for plaque disruption appears to be largely determined by the size of the lipid-rich antheromatous core, the thickness of the fibrous cap covering the core and the presence of ongoing inflammation within and underneath the cap. Inflammatory cells may play a critical role in plaque disruption through the elaboration of matrix degrading metalloproteinases or MMPs (collagenases, gelatinases, stromelysins and matrilysin) and by inhibition of function and survivalof matrix-synthesizing smooth muscle cells. Inflammatory cells may also play a critical role in triggering thrombosis following plaque disruption through the tissue factor pathway. In addition, stresses resulting from hemodynamic and mechanical forces may precipitate plaque disruption, particularly at points where the firbrous cap is weakest, such as at its shoulders. The degree of thrombosis following plaque disruption is determined by the thrombogenicity of the disrupted plaque, disturbed local rheology and systemic thromnotic-thrombolytic milieu. Surges in sympathetic activity provoked by sudden vigorous exercise, emotional stress-including anger, orcold weather, may also trigger plaque disruption. These observations hav led to the concept of plaque stabilization as a new clinical strategy fo- the prevention of acute coronary syndromes. Plaque stabilization can be achieved through pharmacologic and lifestyle-modifying interventions that reduce vulnerability to plaque disruption by altering plaque composition and/or inflammatory activity ithin the plaque.

DISLOCATION OF THE FIRST-METATARSOPHALANGEAL JOINT WITH FRACTURE OF FIBULAR SESAMOID

Clinical Orthopaedics and Related Research 1999;359:209-212

Altaf Hussain, MS, MCh

Dorsal dislocations of the first metatarsophalangeal joint are classified by jahass into two types. In Type I, the hallux with the intact intersesamoid ligament dislocates dorsally over the metatarsal head. Such cases in the literature have been irreducible by closed manipulation. In Type-2 the hallux is dislocated dorsally with rupture of the intersesmoid ligament, resulting in wide separtion of the sesamoids (Type 2A) or a transverse fracture of one or both sesamoids (Type 2B). The importance in classifying these injuries allows one to predict whether closed reduction will be successful as in Type 2. The patient reported had a fracture of the fibular sesamoid in addition to dislocation of the hallux. The clinical findings were consistent with Type I injury, including an intact intersesmoid ligament, but the radiographs showed, in addition to the dislocation, that there was a fracture of the fibular sesamoid. Reduction was achieved surgically through a dorsal approach. Although such injuries have been unreported previously, Type 1 injuries may be associated with a fracture of the fibular sesamoid but without rupture of intersesamoid ligament, so the injury reported is classified as Type 1A.

CONFERENCE REPORT

International Conference on Recent Advances in Medicine - ANUPDAE. Held at Srinagar Kashmir August 21-22, 1999 under the auspicious of Govt. Medical College, Srinagar Kashmir, Medical Council of India (MCI) and American College of Physicians (ACP-ASIM).

International conference on Recent Advances in Medicine - An update, 1999 organised by Govt. Medical College, Srinagar under the auspicious of Medical Council of India and ACP-ASIM was held on 21-23 August 1999 at S.K.I Convention complex (Centur Hotel) Srinagar. The conference was inaugurated by the Hon'ble Chief Minister of J&K State pro-vice Chancellor of Kashmir University). Prof. Phoola Kaul, Principal/Dean, Govt. Medical College, Srinagar (Chairperson) who rendered welcome address, followed by Prof. F.A. Khan, Regent American College of physicians (course Director from USA) who introduced CME programme and presented momento on behalf of ACP-ASIM to Prof. M.S. Khuroo (Ex-Director SKIMS), Prof. Mehraj-u-Din (Director SKIMS) Prof. G.M. Malik (Chief Editor JK-Practitioner) and Dr. M.A. Kamili (Joint organisting secretary) for their best contributions and Research in Medical Sciences, Health care and promoting CME programme; Dr. S.M. Kamal, Hon'ble Medical Education Minister, J&K State (Patron) besides welcoming the delegates, appreciated the role of faculty to render best services as well as maintain high standard of education under the difficult conditions and requested the Hon'ble Chief Minister to help immediately in solving all the pending problems faced by his ministry and the institutions. Dr. Farooq Abdullah, Hon'ble Chief Minsiter highlighted the role of doctors to provided best care to the poor patients of the state as well as continue to produce best generation of medical graduates so that they do not only maintain our prestigious institutions in the state but contribute at National and International Level. He also announced a high power technical committee headed by Dr. S.N. Ahmad Shah alongwith ex-Principals of G.M.C. Srinagar and Jammu to give immediate and concrete new health policy within a period of 2 months so that difficulties faced by Medical Department are immediately solved. At the end Dr. G.M. Malik, Organising secretary gave a brief note on highlights of the conference, difficulties faced by the faculty and their solution and thanked all the speakers, Guests, Deligates, Media, Doordarshan, Radio Kashmir and staff of S.K. Convention Complex for participating and supporting all the deliberations. The inaugural function was followed by scientific session on Pulmonary Medicine and Radiology-Imaging. There was cultural programme organised by Medical College students in collaboration with Director Commercial Services Radio Kashmir Srinagar in the evening followed by a dinner for all those participating in the conference.

On 2nd day there were parallel session on Meet the Professor, Gastroenterology, Cardiology, Pulmonology, Intectious diseases, women health issues etc. from morning till evenin. At the end there was a G.R. Memorial lecture on delivered by professor Farooq A. Khan. It was presided by Dr. S.N. Ahmad Shah, Ex-Principal/Dean, GMC Sgr. and Prof. G.Q. Allaqband, Ex-Principal/Dean, G.M.C. Srinagar. Besides 600 deligates there was a nice who interaction between the old students and their teachers analysed the contributions made by ex-Professors/teachers to Medical College, Srinagar.

On 3rd day NRI faculty visited department of Radiology, Gastroenterology, CCU/ICU of SMHS Hospital Srinagar and then in afternoon they visited various departments of SKIMS Soura. The evaluation reports from the deligates were dvery much encourageing and majority asked for more such CME programme every year. Professor F.A. Khan, Regent ACP in his letter to MCI has been very mcuh impressed by the CME programme, cultural programme as well as the arrangements of the organising committee. The guest speakers were presented momento on behalf of organising committee. The function received full coverage from the state as well as National Doordarshan, Radio Kashmir and the press during all these days.

Prof. G.M. Malik Organising Secretary G.M.C. Sringar

Copy of the Letter from Dr. F.A.Khan Course director to Dr. Sachdeva Secretary Medical Council of India MACP dated 27th August 1999)

Dear Dr. Sachdeva:

I was delighted to participate in the conference jointly sponsored by Medical Council of India/Government medical School/American College of Physicians-American Society of Internal Medicine in Srinagar, Kashmir on August 21st and 22nd, 1999.

The Lectures were of high quality; the attendance and interest of the over -400 registrants were excellent. The faculty, mostly comprised of NRI's, were very pleased with the overall program.

On behalf of the faculty, I wanted to extend our thanks to you for making this conference possible. We looked forward to working with you in the future.

Sincerely Yours

F.A.Khan, M.B.; MACP Course Director

DR. GHULAM JEELANI DHAR, M.D.

Born, raised, and educated in Srinagar, the capital city of Jammu & Kashmir, Dr. G.Jeelani Dhar came to the United States in June 1966 to join Worcester City Hospital, Worcester, Massachusetts, as a medical intern. He spent the next seven years in Minneapolis, Minnesota, as a graduate student at the Unviersity of Minnesota; a medical resident at the University of Minnesota-affiliated hospitals; an instructor in the Department of Medicine, University of Minnesota; Medical unit for Teaching and research inInternal Medicine at Northwestern Hospital. During this time, Dr. Dhar worked with the late Dr. Cecil James Watson on bile pigments and porphyrins and was instrumental in developing and establishing IV Hematin treatment for acute porphyric attacks, for whih no definitive treatment had been developed. This led to two landmark publications in the Annals of Internal Medicine in 1973 and 1975 and a subsequent first prize of the 1975 Annual Resident-Fellow Competition Award of the Chicago Society of Gastroenterolgoy. In 1974, Dr. Dhar joined the gastroenterology section at the University of Chicago, an association that has continued until the present time. During 1974-76, Dr. Dhar completed his fellowship training in gastroenterology and became certified by the American Board of Internal Medicine with a subspecialty in gastroenterology. At the same time, he started working with Dr. Irwin H. Rosenberg on elucidating the mechanism of intestinal folate trnasport and its inhibition by sulfasalazine. The following year, Dr. Dhar was appointed a research associate/assistant professor in the Department of Medicine, gastroenterology section, and, along with Professor Ference J. Kezdy in the Department of Biochemistry, worked to define the kinetics of the intestinal folate transport. in 1977, Dr. Dhar moved temporarily to Milwaukee to the gastroenterology section of the Department of Medicine at the Medical College of Wisconsin. in addition to clinical and teaching responsibilities, Dr. Dhar continued his work on folate transport. After three years in Milwaukee, Dr. Dhar moved back to Hyde Park in Chicago to set up a part-time is a medical director of gastroenterology at Doctors Hospital of Hyde Park and a clinical associate professor in the Department of Medicine, gastroenterology section, University of Chicago.

Dr. Dhar has been a life member of IMA for more than 10 years. In 1994, he was the lcoal chairman of the 27th annual conventionheld in Chicago.

In the subsequent years, he was elected secretary, vice president, and president-elect of the IMA. Dr. Dhar assumed the presidency of the IMA at the general body meeting held on July 28, 1997, at the annual convention in Amman, Jordan.

Dr. Dhar is a dynamic person who has been involved with Islamic activities at local, national and international levels. In his hometown of Chicago, among other things, he has been instrumental in bringing the weekly Tv program "Islam" and he also serves on the board of directors of the Muslim Community Center. We look forward with great expectation for his year of presidency.

Hand Bookon Medical Emergencies (1999 Edition) Edited by Dr. Mohammed Yousuf, Ex. Prof/HOD Medicine, G.M.C. Srinagar.

The new edition "Hand Boor on Emergencies in Medicine" edited by Dr. Mohammed Yousuf, Ex-Prof/ HOD Medicine is better in all respects than that of previous one. The author has taken good care to update all aspects of emergencies in Medicine as well as diagnostic methods. However, the photographs of x-ray's etc. need improvement. I recommend this book for students as well as for clinicians/Medical teachers.

(Dr. G.M. Malik) MD, FACG, Prof. Deptt. of Medicine, Govt. Medical College, Srinagar.

Manual of Practical Medicine (1998), Edited by: Dr. Alagappan. Published by JAPYEE Brothers.

Dr. Alagappan, an eminent physicians and experienced teacher has written a nice text book which deals with the current clinical Medicine. The book has covered all clinical diseases alongwith relevant and latest diagnostic techniques in various chapters. A good number of coloured photographs of patients, endoscopy, CT and X-Ray's have been included. Photographies have been nicely scanned book has been written in a very simple and understandable language. Printing and papers in also good. I congratulate the author for his hard work to edit this nice updated book at reasonable cost. I would recommend this book for all undergraduates as well as postgraduate students Medical teachers an practitioners.

(Dr. G.M. Malik) MD, FACG Prof. Deptt. of Medicine, Govt. Medical College, Sgr.

Conference Calendar:

1. ***International Institute of Islamic Medicine and The Islamic Medical Association of North America announces. 5th International Convention on" Islamic Medicine in the 21st Millennium" at Hyderaliad India on Jan 14-17-2000.*** For details Contact Dr. M. Fakhrudin Princess Durra Shehvar Children's and General Hospital - {urani Haveli Hyderabad. Tel. 520480/ 526155/520548.
2. ***Annual Conference of Indian College of Cardiology at Srinagar Kashmir, June 2-4-2000.*** For Detail Contact. Dr. G.Q. Allaqaband, Organising Secretary 52, - Balgarden Srinagar, Kashmir. Telephone 474532. E-mail zakhatib@vsnl.com.
3. ***20th Annual Conference of Northern Chapter of Association of Surgeons of Indian NC-ASICON-99.*** Venue:- Hotel Meghdoot, Chaura Maidan, SHIMLA ***Dates: 12-14 November 1999.*** For Details Contact: Prof PC Sood, Organising Secretary Prof. & Head, Deptt. of Surgeon I.G. Medical College Shimla - 171001. Res. 240316, 243316. Fax. 0177-2583398. E-mail PC-sood@hotmail.com.

Obituary

Dr. Abdul Majid Rather (1951-1999)

Dr. Abdul Majid Rather was a noble, honest hard working, ENT Surgeon who served the poor with all the dedication. In his death we have lost an able ENT surgeon. He made a great contribution in the patient care and education of the medical students. He will be remembered for his honesty and humbleness. He was a deeply religous man. He was very nice to both his superiors and subordinates. The greatest tribute to his memory will be that we follow the principles and path laid down by him. Dr. Abdul Majid passed his MBBS from Govt. Medical College, Srinager in 1973. He joined ENT Department of Govt. Medical College, Srinagar as a Lecturer in 1980 after his postgraduation at Maulana Azad Medical College, New Delhi. He was promoted as Professor in 1998.

Dr. Abdul Majid Rather was born on 2nd September 1951 at Mehmood Abad, Doru, Islamabad, Kashmir. He left for heavenly abode from 25th September 1999, at the age of 48 years. He is servived by his wife and three children. May his soul rest in peace and God grant us all enough strength to bear this great loss.

From:

1. *Prof. Abdul Ahad* HOD, ENT Deptt. Govt. Medical College, Srinagar.
2. Prof. Phoola Koul, Principal Govt. Medical College, Srinagar.
3. *President/Secretary* Indian Medical Association (Kashmir Branch), Medical Faculty Association (MFA). Govt. Medical College, Srinagar.
4. *Chief Editor & Editorial Board* JK-Practitioner, Srinagar Kashmir.

International Conference on "Recent Advances in Medicine - An update Held at Srinagar - Kashmir August 21-23, 1999

PHOTO FEATURE

***Inaugral Address**: 1 Dr. Farooq Abdullah, Hon'ble Chief Minister J&K addressing the gathering on the inaugration of the Conference on 21-8-99*

***In the Forefront**: 2 Course Director Dr. Faroque A. Khan with Dr. M.A. Kamili Joint Secretary & Dr. G.M. Malik Organising Secretary.*

***Award for Speakers** : 3 & 4 Prof. SN. Ahmad Shah handing over momentoes to Dr. Sabiha Raoof (USA) and Dr. Parmood Gujral (Lucknow) Dr. G.Q. Allaqaband, Dr. M.S. Khuroo, Dr. M.A. Kamili & Dr. G.M. Mir can be seen in the background (21-8-99)*

***Discussing**: 5 L-R Dr. S. Malik, Dr. Qazi M. Syeed, Dr. A.R. Mir Dr. Arfia Kha, Dr. F.A. Khan, Dr. M.Bukhari, Mr. S. Fazili, Dr. Tanveer Mir, and Dr. Saima Qazi*

***Relaxed and Happy**: 6 Front. Dr. Arifa Khan, Dr. Neelofer Qadri. Back. Dr. Bilquees Jamila, Dr. Tanveer Mir, Dr. S. Hakim, Dr. Shahida Aga and Dr. Rashida Parveen Chisti*

IN EXPERIENCE
O
The low osmolar non-ionic
X-ray contrast medium

- A universal contrast medium for all examinations
- The most widely documented X-ray contrast medium with over 4,000 publications
- Over 150 million examinations carried out worldwide with **OMNIPAQUE**®
- Wide range of presentations and concentrations

We Created OMNIPAQUE®
The Standard of Excellence in Diagnostic Imaging

Nycomed
Amersham

Nycomed Asia Pacific Pte Ltd., Liaison Office India
AD 46 First Street Annanagar Chennai - 600 040 India. Tel: 91 44 628 9030/628 9031
Fax: 91 44 628 9033 Email nycomed@md2.vsnl.net.in